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Materia Medica Pharmacology and Therapeutics for Nurses

By

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PREFACE

THE plan of this book resulted from many trials of various ways of teaching Materia Medica to students of nursing and was developed gradually in connection with the author's class work.

In the primary writing of the manuscript almost all the drugs in the U. S. Pharmacopœia and in "New and Non-Official Remedies" were included, but it was evident that this would make a book of more than 600 pages and therefore a large number of those not included in "Useful Drugs" or in common use were omitted or merely their preparations and dosage mentioned; for, on consideration, it did not seem necessary to require students of nursing to study the action of drugs that are seldom used or which the American Medical Association does not consider essential for students of medicine to memorize. Blank pages are inserted at the end of this book for a memorandum of new drugs that come into such frequent use that they are worth remembering.

In compiling this book a large number of medical books and magazines were consulted, but those most frequently referred to were: The American Journal of the Medical Sciences; Progressive Medicine; The Journal of the American Medical Association; Useful Drugs; New and Non-Official Remedies; The Pharmacology of Useful Drugs, Robert A. Hatcher, and Martin I. Wilbert; Materia Medica, Pharmacology, and Therapeutics, Bastedo; Pharmacology and Therapeutics of The Action of Drugs, Arthur R. Cushny; A Manual of Pharmacology, Sollmann; The Action of Drugs, Sollmann; Handbook of Antiseptics, Dakin and Dunham; The National Formulary; Serum and Vaccine Therapy, Hewlett.

AMY E. POPE.

SAN FRANCISCO, CALIFORNIA.
January, 1921.

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MATERIA MEDICA, PHARMACOLOGY AND THERAPEUTICS

A TEXT-BOOK FOR NURSES

INTRODUCTORY

NAMES OF THE BRANCHES OF SCIENCE CONCERNED WITH THE STUDY AND USES OF MEDICAL MATERIAL

Materia medica is the science or study of the origin and of the chemical and physical properties of medical material, *i.e.*, the substances used for the cure and prevention of disease, such as drugs, antitoxin serums, and vaccines. In the past, the term materia medica has been very commonly used to include the study of the action of drugs, but, according to the accepted meanings of the terms materia medica and pharmacology, this is not correct.

Pharmacology is the science or study of the action of medical materials upon living organisms.

Therapeutics implies the treatment of disease and, as there are many methods of treatment, there are several branches of therapeutics; *e.g.*, drug therapy—*treatment with drugs;* serum therapy—*treatment with serum;* heliotherapy—*treatment with light;* hydrotherapy—*treatment with water;* psychotherapy—*treatment by influencing mental conditions, this includes suggestion and hypnosis.*

Toxicology is the science which treats of poisons—their nature, the symptoms they produce and the means of overcoming or preventing their ill effects.

STANDARD BOOKS DEVOTED TO THE ABOVE SUBJECTS

The Pharmacopœia is a book that has for its object the standardizing of the drugs in common use by physicians.

Most of the nations whose physicians have contributed to the advance of medical science have a national pharmacopœia so that there is the British Pharmacopœia, the French Pharmacopœia, the United States Pharmacopœia, etc. The latter is usually designated in writing as the U.S.P. This is revised every ten years by the U. S. Pharmacopœial Convention. The word *non-official* after a drug signifies that it is not as yet listed in the Pharmacopœia.

The National Formulary is a book issued by the American Pharmaceutical Association to standardize some drugs in common use that are not as yet in the Pharmacopœia.

New and Non-official Remedies is the name of a book published by the American Medical Association in order to make known new drugs that physicians have stated to be of value.

Useful Drugs is a book published by the American Medical Association and revised yearly. It contains a list and short description of drugs, old and new, that investigators have found to be of value. One purpose for its publication is to direct the attention of medical students to those drugs which it is most important for them to study.

WHAT STUDENTS OF NURSING SHOULD LEARN ABOUT DRUGS

1. Students should learn the dosage of the important drugs, especially the more poisonous ones and those which are likely to be prescribed in emergency. This knowledge is necessary, not that nurses may know how much to give without a doctor's order, but because it will prevent misunderstanding orders.

2. They should learn the symptoms of overdosing and of poisoning induced by all important drugs in common use and also the remedies for poisoning.

3. They should have some knowledge of the physiological effects of the more important drugs and of their therapeutic uses. There are at least two reasons for such

knowledge: (1) Unless nurses know the action of the drugs they give, they will not know what symptoms to watch for nor be able to give an intelligent report of the results following the administration of a drug. (2) There are few people who can do really good intelligent work unless they are enough interested in it to know what they are doing.

4. It is exceedingly important for nurses to know how to make solutions of different percentages and how to estimate the quantity of a drug to use when the dose ordered is of a different strength from that of the preparation on hand.

5. Of interest, though of less importance than the other items mentioned, is a knowledge of the origin of drugs (whether they are derived from plants, animals, minerals, etc.) and of the nature of the different preparations, *e.g.*, extracts, fluidextracts, tinctures.

HOW THE STUDY OF DRUGS MAY BE FACILITATED

The class-work for the study of drugs is purposely left until that of chemistry and of physiology have been completed, but the students in the meantime, as well as while they are actually studying the subject, should read the descriptions of the actions of the drugs they hear about and give and be on the alert to observe the results on those taking the drugs. Making a *mental note* of the dosage when administering drugs and looking up that of drugs heard about is a far easier way of memorizing dosage than of studying it for class. A very important point for students to realize with regard to the study of drugs is that there is no other study that is more helped by concentrated thinking and by comparison, for the physiological effects of a drug give the clue to both its therapeutic uses and the symptoms of poisoning so that if the physiological effects are thought of it will be easy to recall the other two items. As will be seen in the section on Toxicology, there is very little difference in the

symptoms of poisoning by drugs of the same class and noting the differences and similarities, rather than studying the symptoms and treatment of each poison as a separate item, will facilitate memorizing the essentials.

Usually the terms action and effect are used as synonyms but, in this book, the word action is applied to what might be called the drugs' primary results upon the affected tissues, and effects, to the consequences of these results. As far as possible, the actions of the important drugs are described before their effects and the pupils are advised, when they begin to study a lesson, to read the whole section describing the drug and then, turning to the description of its action, see if they remember the therapeutic and toxic effects of each action and if they understand the reason for each effect. In the case of a number of drugs, it will then only be necessary to actually memorize the actions and those effects which were not thought of, because recalling these will usually bring back to memory the other important data. When reference is made to a drug previously described, the students, before turning to the article referred to, should try and recall it, because the effort of recall is likely to give rise to a more lasting memory than mere rereading.

DRUGS AND THEIR PREPARATION

DERIVATION AND NATURE OF MEDICINES

Medicines are obtained from both organic and inorganic matter. Those of organic origin are derived both from plants and animals. The plant substances used as drugs are obtained from different parts of plants, *e.g.*, some drugs are obtained from the leaves, others from roots, others from seeds, etc. Those of animal origin with a few exceptions, such as cantharides, which is prepared from a species of fly, are preparations of glands or their extracts, or of blood serum.

A large number of the newer drugs are prepared from coal and wood tars and from crude petroleum.

The tars are dark, semi-solid products of the destructive distillation[1] of coal and wood. They consist of mixtures of a large number of substances that can be separated from each other by fractional distillation,[1] for they all have different boiling points. The majority of the constituents of tar are hydrocarbons (compounds of hydrogen and carbon) such as benzene, napthalene and anthracene, but they also contain some compounds which have small amounts of other elements, from which carbolic acid, anilin and other important substances are derived. Most of the tar derivatives are very active chemically, *i.e.*, they can be easily made to unite with different elements or compounds and thus a very large number of drugs and other substances have been prepared from them synthetically.

[1] The process of boiling and thus vaporizing a substance and condensing the vapor. Destructive distillation is that in which a substance is decomposed and new products formed during the decomposition. Fractional distillation is that in which a constituent of a mixture that has a different boiling point from the other constituents is removed by maintaining the mixture at the boiling point of that constituent.

Crude petroleum, like coal, has been formed in the depths of the earth by the decomposition of organic matter. It is a physical mixture of substances, similar to those of the tars which, like them, can be separated by fractional distillation.

A number of substances which resemble or are identical with the products of the distillation of the tars and petroleum can be **obtained by the distillation of certain balsams, resins, and volatile oils of plants.** Thus, toluene is obtained by distillation of tolu balsam, as well as that of coal tar; thymol, which is similar to carbolic acid, is obtained from the oil of thyme; and salicylic acid, which also resembles carbolic acid, may be obtained from the oils of wintergreen and birch-bark or prepared synthetically from coal tar products.

DRUG CONSTITUENTS

Drugs may consist of simple chemical compounds, such as salts, acids, etc., or of combinations of compounds. All the constituents of some compounds are active but others contain both inert and active substances. The inert substances (*i.e.*, those which are not chemically active) may be either substances that are used to dilute the drug or to facilitate its administration or, in the case of drugs of plant origin, they may be substances such as the cellulose and mineral matter of the plant. Substances which act either upon the body tissues or other ingredients of the drug are termed *active constituents* and, of these, those to which the physiological actions of a drug are due are called *active principles.*

The active principles are sometimes extracted from the crude drug and used separately, but, sometimes the whole drug is used. Some drugs of plant origin, contain more than one active principle and, in some of these, the active principles have different actions. In such cases the action of the whole drug is more or less different from any of its active principles, but, if all the active principles have the same action, that of the whole drug will be similar, but,

unless taken in large amounts, weaker because of the inert substances present.

The more important active principles of drugs are classed as: Alkaloids, acids, salts, glucosides, saponins, volatile oils, stearoptens, resins, oleoresins, balsams, enzymes, tannins and oils.

Alkaloids are organic, nitrogenous substances with an alkaline reaction. They combine with acids to form salts and it is in this form that, when extracted from the crude drug, they are used in medicine.

Acids are substances with a sour taste that turn blue litmus red and combine or interact with metals, metal oxids, hydroxids, alkalies and alkaloids to form salts. All acids have one or more hydrogen atoms in loose combination and they part with this hydrogen when they interact with other compounds. It is to this replaceable hydrogen that they owe their acid characteristics. The acids derived from organic substances all have what is known as an organic acid radicle,[1] which is COOH. This when oxidized breaks down to carbon dioxid and water.

Hydroxids are compounds that contain an OH radicle. The majority of hydroxids, but not all, are alkalies, the alcohols, for example, have not an alkaline reaction, but they have one or more OH radicles and they combine with acids to form what are known as *ethereal salts or esters.*

An alkali is generally defined as a substance that forms salts with acids and soaps with fats and turns red litmus blue.

The salts formed by the interaction of an acid and an alkali may be either acid, alkaline or neutral (*i.e.*, neither acid nor alkaline). Some of these salts owe their properties to their acid radicle—*e.g.*, the bromides and iodides —others to their alkaline radicle, *e.g.*, sodium carbonate. The neutral salts of the alkalies generally owe their effects to what is known as a salt action, described page 47.

[1] By a radicle, it will be remembered, is meant a group of elements forming a part of a molecule that act as a single atom in a chemical reaction and are not easily divided.

The salts of the metals owe their effects chiefly to their metal element and the alkaloids to their alkaloid compound, but the acid modifies the nature of these salts to some extent, especially as regards their solubility and, therefore, some salts with similar bases, but different acids, may be more readily absorbed and more active than others.

Glucosides are substances that, when decomposed, yield glucose or other sugar in addition to other substances.

Saponins are glucosides that have soap-like properties, *i.e.*, they foam when mixed with water and they are irritant to mucous membranes.

Volatile oils, the resins, stearoptens and balsams are described later, pages 274 and 366.

Tannins are described under astringents (p. 293) and enzymes on page 227.

PHARMACEUTICAL PREPARATIONS

Some drugs are employed in their natural form, but others are prepared for use in various ways. The names and nature of the important preparations are as follows:[1]

Solid Preparations

Bougie—a taper-shaped preparation of medicated wax, used in the same manner as a suppository.

Cerate (*ceratum, cerati*)—a preparation for external use in which the drug is incorporated in white wax.

Confection (*confectio, confecti*)—the drug is mixed with aromatic substances and honey or syrup in order to disguise its taste.

Extract (*extractum, extracti*)—a preparation made by extraction; *i.e.*, the crude drug is mixed with a liquid in which the cellulose and woody fiber are not soluble, but the active principles are. This is filtered, in order to remove the insoluble material, and the liquid of the filtrate is then evaporated. The solid material remaining

[1] The English name is given first, then the Latin name and then the genitives of Latin names commonly used in prescription writing.

represents the extract. This contains the active principles, but also other soluble material extracted from the crude drug, and thus the action of an extract is not as powerful as that of active principles, but it is generally four or five times more so than that of the crude drug.

Lozenge—a flat disc consisting of tragacanth or other demulcent material in which a drug is incorporated. It is intended to be dissolved in the mouth.

Ointment (*unguentum, unguenti*)—a soft preparation in which the drug is held in a fatty base, such as lard, lanolin (fat obtained from the wool of sheep) or vaselin, which is melted at or about the temperature of the body. Most ointments are used to obtain the effect of the drug at the point of its application but a few contain drugs that can be absorbed through the skin.

Pill (*pilula*)—a small, rounded or oval preparation of a drug in solid adhesive substance. Pills are often coated with some substance to disguise their flavor, as sugar or chocolate, or, when their action is not wanted until they reach the intestine, with a substance such as keratin, which is not readily soluble in the gastric juice. Pills are likely to become very hard and insoluble when they are kept for any length of time and, in such case, they may be expelled undissolved in the feces.

Plaster (*emplastrum, emplastri*)—a preparation in which the drug is incorporated in some adhesive substance which is spread in a thin layer on muslin, paper, moleskin or similar substance. Plasters are intended for application to the skin.

Powder (*pulvis, pulveris*)—a finely powdered drug.

Suppository (*suppositoria, suppositorium*)—a preparation in which the drug is incorporated in some substance, usually cocoa-butter, which maintains its shape at ordinary temperatures, but will melt at the temperature of body cavities. Suppositories are shaped according to the cavity into which they are to be inserted, those for rectal use are cone-shaped, those for the urethra, thin pencil-shaped; those for the vagina, round or elliptic shaped. The drug

of a suppository is generally intended for its local effects, but, occasionally, a drug that is readily absorbed through mucous membranes is given in a rectal suppository.

Tablet (*tabella*)—a small moulded, compressed preparation of a powdered drug. Tablets in which the drug is mixed with sugar of milk are termed *triturates*. Those of effervescing salts are called *vescettes*.

Troche (*trochiscus*)—same as lozenge.

Liquid Preparations

Collodion (*collodium*)—a solution of a drug in collodion. Collodion is a solution of gun-cotton in ether and alcohol. It evaporates readily leaving a contractile film over the surface to which it is applied.

Decoction (*decoctum, decocti*)—a liquid preparation of a drug prepared by boiling the crude drug in water and straining it to remove the residue.

Elixir (*elixir*)—a sweetened, aromatic, hydro-alcoholic liquid.

Emulsion (*emulsum, emulsi*)—a solution of an oily substance in which the oil is broken into fine globules and held in suspension in water by means of some viscous substance such as acacia.

Fluidextract (*fluidextractum, fluidextracti*)—an alcoholic or hydro-alcoholic preparation of a drug made by extraction, of which each c.c. contains 1 gram of the drug or, each minim, 1 grain.

Glycerite (*glyceritum, glyceriti*)—a solution of a drug in glycerine.

Infusion (*infusum, infusi*)—a solution of a drug made by steeping the crude drug in boiling water and, when cold, straining it. (Compare with decoction. What is the difference between the two preparations?)

Liniment (*linimentum, linimenti*)—a preparation for external use consisting of, as a rule, irritant drugs in an oily or alcoholic liquid.

Mixture (*mistura, misturæ*)—a preparation in which an insoluble drug is held suspended in water by means of a

viscid substance. A mixture must always be shaken before being poured.

Solution (*liquor, liquoris*)—a preparation in which one or more non-volatile substances are dissolved in water. The term solution, but not liquor, is used also for any liquid containing dissolved material.

Spirit (*spiritus*)—a solution of a volatile substance in alcohol.

Tincture (*tinctura, tincturæ*)—an alcoholic or hydro-alcoholic extract of a drug. Unless otherwise stated, the strength of a tincture is 10 per cent. Thus, except that they are weaker, tinctures are the same as fluidextracts and, in the case of most drugs, the dose of a tincture is ten times larger than that of the fluidextract. Two so-called tinctures, tincture of iodine and tincture of ferric chloride, are incorrectly named for they are not prepared by extraction, the drugs being merely dissolved in the alcohol and, therefore, the iodine is a spirit and the ferric chloride an alcoholic solution.

Water (*aqua, aquæ*) a solution of a volatile substance in water. (Compare: Solution (liquor) spirit, and water.)

Wine (*vinum, vini*)—a solution of a drug in white wine.

NAMES AND NATURE OF SPECIAL CONTAINERS FOR INCLOSING MEDICINE

Cachet—two small lens-shape pieces of rice paper, the borders of which can be stuck together after a dose of medicine is placed in the center. The paper is dissolved by the gastric juice and the drug set free.

Capsule—a small case for inclosing a dose of medicine. Those in common use for internal administration are made of gelatin, which is dissolved by the gastric juice, but when a drug is to be used that would be changed by the gastric juice or which would have an undesirable effect upon the stomach, the drug is sometimes enclosed in capsules made of keratin (a substance obtained from horn) which, though

dissolved by the alkaline intestinal juices, is not readily affected by the acid gastric juice.

Ampule—a capsule of thin glass in which a dose of medicine is enclosed, the top can be easily broken off when the drug is required. Sterile doses of drugs for hypodermic use are sometimes put up in this way.

Sterule—same as ampule.

THE ADMINISTRATION OF DRUGS

Drugs are used both for their local effects and for their effects after absorption.

By local effect is meant the results of a drug's action at the site of its application. The parts to which a drug can be applied locally are: The skin; the conjunctiva and cornea; the mucous membranes of the respiratory, alimentary and genito-urinary tracts; wounds; tissues that can be reached by a liquid forced through a hypodermic needle. For use on the exterior of the body drugs are often incorporated in ointments, cerates and plasters, because these adhere to the skin and do not dry readily. For use in the rectum and genito-urinary passages drugs are very commonly applied in the form of bougies and suppositories, these preparations being easily inserted and having the same advantages as ointments and cerates. For treatment of the throat and mouth, medicines are often used in lozenges or troches for, as these dissolve slowly, they allow of the drug being kept in contact with the parts for a longer time than if it is swallowed; also, in these parts, drugs are very commonly used in washes, gargles, sprays and the like and volatile drugs are used as inhalations, either with or without steam. For action in the stomach and intestines, drugs may be swallowed or, as in the treatment of all accessible body cavities, given in some form of irrigation (*e.g.*, douche, clysis, enema, lavage).

Absorption of Drugs.[1]—If a drug is not readily absorbed its value for local effects will, as a rule, be increased, for it will then remain longer in the part where its action is desired. On the contrary, properties that allow of ready

[1] The pupils should read the section on absorption in their text-books of Physiology or Physics, if they are unable to recall what they have learned of this process.

absorption are valuable for drugs that are to act after their absorption. The nature of these properties, in the case of some drugs is not entirely understood but the properties of diffusibility and solubility are influential factors and practically all volatile drugs are readily absorbed and, other things being equal, the more soluble a drug is the more readily it is absorbed, while insoluble substances are very imperfectly absorbed, if at all, through animal membranes.

The absorption of even soluble matter is hindered by: (1) The insoluble substances,[1] such as cellulose and gums, present in crude vegetable drugs, thus crude drugs, and even extracts, are not absorbed as quickly as the separated active principles and, therefore, will take longer to produce systemic effects (those occurring after absorption) but, if they have any local actions, these will be prolonged; (2) mixture with mineral oils and mucilaginous substances such as acacia and tragacanth. Alcoholic preparations **are absorbed quicker** than aqueous, both because alcohol is absorbed more readily than water and because, as will be seen later, alcohol increases the amount of blood in tissue with which it comes in contact, which favors absorption. Solution in vegetable and animal oils increase the absorbability of some drugs.

The different tissues vary considerably in their power of absorption: Very few drugs are absorbed through the skin; they are absorbed more readily through mucous membranes, but the membranes of different parts show differences in their power of absorption; for instance, when given by rectum, drugs are not as readily absorbed as when given by mouth. It is only the membranes of the respiratory and alimentary tracts that are utilized as channels for the absorption of drugs, but it must not be forgotten that absorption takes place through that of the genito-urinary tract, for patients have been poisoned by excessive

[1] In materia medica, the term insoluble substances is applied to matter that cannot be dissolved by the solutes commonly used for dissolving drugs nor by the gastric nor intestinal juices.

amounts of drugs used in these parts for their local effects. Absorption takes place more rapidly from subcutaneous tissues than from mucous membranes and from deeper (intramuscular) tissues than from subcutaneous. Gaseous drugs are rapidly absorbed through the lungs, but, of course, these are the only kind that can be administered in this way.

For their effects after absorption, drugs may be administered in any of the following ways:

1. Through the skin: For this method of administration, the drugs are used in oils or as ointments. Their absorption through this channel is aided by rubbing (*i.e.*, inunction) but it is limited and uncertain.

2. By inhalation: Only gaseous drugs are given by this method.

3. By mouth.

4. By rectum: This method of administration, however, is not commonly used, except for local treatment and, occasionally, in proctoclysis, for the drugs are likely to be expelled and their absorption is uncertain.

5. By hypodermic and intramuscular injections. The latter method is used for the more irritant drugs, because, (1) as they are more rapidly absorbed from the deeper tissues, they are less likely to injure the cells; (2) they cause less pain for there are fewer sensory nerve-endings in the deeper parts than in, and directly under, the derma. However, very irritant drugs cannot be given even intramuscularly, because irritation, beyond a limited degree, destroys tissue. Drugs are given in these ways when: (1) Rapid effects are required; (2) the patient can not or will not swallow, or is nauseated or has diarrhea; (3) the gastric or intestinal juices change the drug, either by digesting it, or by the action of the hydrochloric acid of the gastric juice or of the alkaline matter in the intestine; or (4) the drug, after absorption, is retained or destroyed in the liver. It will be remembered that, with the exception of fats, material absorbed from the stomach and intestine passes, via the portal vein, to the liver.

6. Intravenously: Only drugs that investigation has shown will not coagulate the blood or cause disintegration of blood-cells can be given in this manner. Those which can be so used are given in this way when instant effects are required and when, as in the case of a few drugs, such as salvarsan, it has been found that they are very irritating to the tissues but do not injure the blood-cells.

As the methods of giving medicine in these various ways and the precautions necessary in their use are described in all text-books of nursing procedures, space will not be taken to do so here, but the pupils should review the chapters devoted to such description in their other text-book and be prepared to answer questions.

In the case of a few groups of drugs the time of administration is of importance when they are given by mouth and, though the doctor usually specifies the time of administration, it is well for nurses to know the more important facts that have to be considered; viz.: Drugs which are altered undesirably by acid[1] and those intended for local effects in the stomach and intestines (this includes cathartics) are usually given while the stomach is empty, *i.e.*, **between meals**; cathartics which act slowly are generally given at night and those which act rapidly, in the morning before breakfast. Drugs intended to improve the appetite and increase the secretion of digestive juices are given shortly **before meals.** Irritant drugs intended for absorption, such as digitalis, arsenic, iron and quinine, are given **after meals** (while there is food to protect the membrane from too severe irritation) and also, as a rule, drugs used to lessen the acidity of the gastric juice.[2] Some authorities believe that when the rapid absorption of drugs is desired they should be given after meals, because there is then an increased amount of blood in the gastro-intestinal membrane, which favors absorption, but others believe that the presence of undigested food hinders absorption, and this is certainly true of alcohol.

[1] Normally hydrochloric acid is only secreted during digestion.
[2] There are exceptions to this rule that will be seen under antacids.

Points regarding the dilution of drugs that require any special preparation by the nurse are given in the sections describing the drugs, there are certain rules however that it is well to emphasize; viz.: Irritant drugs should be well diluted and those not intended for local effects, when given by mouth, are very commonly diluted with a demulcent such as milk or syrup. The diluents used should be either cold or hot, not tepid. When rapid absorption is wanted, drugs are to be diluted in a large amount of water or, if used in solid form, a copious drink should be taken afterward. On the contrary, when absorption is to be delayed, a smaller amount of diluent is used as a rule, and mucilaginous ones are sometimes prescribed. Syrups, such as cough mixtures, are not diluted. For use by children, solid preparations are best powdered and given in jelly or in flavored syrup. Drugs should be given only in liquid form to the unconscious and insane. As a rule, under such conditions, drugs are given by hypodermic but a small quantity of medicine can generally, if necessary, be given to an unconscious patient by dropping it on the back of the tongue from a spoon.

DOSAGE

By the dose of a drug is meant the amount ordinarily required to produce therapeutic effects in an adult. The smallest dose that has been generally found to be capable of doing so is termed the *minimum dose* and the largest dose that can ordinarily be used without risk of inducing too pronounced effects is known as the *maximum dose.*

Factors upon which the choice of the size of the dose depend and which, in some cases, call for even larger or smaller doses than those within the therapeutic range are as follows:

1. **Size of the Individual.**—The smaller the person, other things being equal, the smaller the dose required.

2. **Temperament.**—People with emotional temperaments are usually more easily affected by drugs, and thus require smaller doses than those of phlegmatic dispositions.

3. **Age.**—Elderly people generally require smaller doses than adults of middle age and small children may be poisoned by doses that are therapeutic for an adult and, the younger the child, the more easily will it be poisoned. Therefore, for patients under sixteen, or thereabouts, the age must be taken into consideration. There are a number of methods used for estimating the dosage for children. The following one, known as *Young's rule* is very commonly used.

Young's Rule for Estimating the Dosage for Children. Make a fraction taking the child's age for the numerator and the child's age plus 12 for the denominator and this will give the proportion of the adult dose that is to be used. For example, if the child is 6 years of age this will be $\frac{6}{18}$, the equivalent of this is $\frac{1}{3}$, thus, for a child of 6, with the majority of drugs, $\frac{1}{3}$ of the adult dose will be used. For example, if the dose of a drug for an adult is 15 grains, that for a child of 6 will be 5 grains. A few drugs, especially opium and its derivatives, have to be given in proportionately smaller doses to children and there are a few that can be given in relatively larger doses.

4. **Sex.**—Women usually require smaller doses than men, this is partly because they are of smaller stature, but also because they are more susceptible to most physiological influences.

Susceptibility and Idiosyncrasy.—For reasons already given and others, the cause of which is often not apparent, some individuals are much more susceptible to the influence of drugs than others; take the well known example of coffee; some people can drink two or three cups before retiring and then sleep soundly while others will be kept awake if they take a very small amount. Some people are so susceptible to the influence of some drug or drugs that toxic symptoms will develop from even moderate therapeutic doses. In such case the individual is said to have an *idiosyncrasy* for the drug.

5. **Tolerance.**—The system becomes accustomed to the action of most drugs and thus, if a drug is used continu-

ously, unusually large doses will be required after a time to get any effect.

6. **Certain diseases and conditions** allow of some drugs being used in larger amounts than usual, for example, a person in pain can take larger amounts of morphine than otherwise; in malaria, larger doses than usual of quinine can generally be taken without experiencing unpleasant effects. On the other hand, some conditions increase the possibility of bad results from a drug, for example, if a person is cyanosed or dyspneic, morphine or any other drug which interferes with breathing may have a bad effect.

7. **Method of Administration.**—In the case of the few drugs that can be given intravenously, smaller doses are likely to be used than for other methods of administration; but this is not always the case for, when this method of administration is resorted to, prompt and strong action is likely to be desired. Larger doses are generally used for rectal than for oral (mouth) administration. Some books advise smaller doses for hypodermic than for oral use, but this is not always customary.

8. **The Nature of the Preparation.**—The active principles of a drug are used in much smaller doses than other preparations, and extracts are used in smaller amounts than preparations of the crude drug. Of the liquid preparations, fluidextracts which, as previously stated, are 100 per cent., are the most potent and, it will be noticed that those of the more toxic drugs are used in very small amounts, usually 1–3 minims; tinctures of the more toxic drugs are 10 per cent.; thus the dose of the majority of tinctures is ten times larger than that of fluid extracts. Infusions, decoctions, syrups, mixtures, etc. are all weaker preparations than tinctures and are thus used in larger amounts.

COMPUTING DOSAGE

Accuracy in the administration of medicines necessitates a vivid remembrance of the tables of weights and measures used in pharmacy and of the rules followed in computing

dosage. A few easy rules to remember for the calculations that nurses have most frequently to make are given on pages 39 to 42. Pupils who need more help than this and the examples given them in class are advised to get the small book entitled "Solutions in Ten Lessons" by Elsie M. Smith.

WEIGHTS AND MEASURES

In pharmacy, both the apothecaries' and the metric systems of weights and measures are used. The latter, however, being more convenient and accurate, is gradually being generally adopted. It originated in France in 1795. According to it, **the meter** is the unit of length, the liter of volume and the gram of weight. A meter is the tenth-millionth part of the distance from the equator to the north pole. The space of a cube[1] one meter long, one meter wide and one meter high, is called a *cubic meter*. **A liter represents** the volume (*i.e.*, the amount of space occupied) of a cube of water at its greatest density (*i.e.*, when it is 4°C.),[2] each side of which measures one decimeter (*i.e.*, one-tenth of a meter); thus the size of a cube representing the quantity known as a liter would be one-tenth of that of a cubic meter. **A gram represents** the weight of a cube of water at 4°C. each side of which measures one centimeter (*i.e.*, one-hundredth part of a meter). Thus a cube representing the weight of a gram would be one-tenth the size of the cube representing the volume of a liter and one-hundredth that of a meter.

[1] A body with six square sides of equal size.

[2] It will be remembered that water, like all other matter is expanded by heat and its density thus reduced and that water also expands when its temperature goes below 4°C., which is why ice is lighter than water and, therefore, floats. Similar weights of different kinds of substances occupy different amounts of space; a pound of lead, for example, is of smaller proportion and will therefore take up less space than a pound of wood. Thus it is necessary to have a standard for comparison and water being the standard used by physicists for other measurements and calculations has been chosen.

The prefixes deca, hecto, kilo (derived from the Greek) are used to denote increases, and the prefixes deci, centi, milli (derived from the Latin, are used to denote decreases). For example:

Millimeter	= 0.001	of a meter
Centimeter	= 0.01	of a meter
Decimeter	= 0.1	of a meter
Meter	= 1.0	
Decimeter	= 10	meters
Hectometer	= 100	meters
Kilometer	= 1000	meters
Myriameter	= 10000	meters

The term cubic centimeter and its abbreviation c.c. are more commonly used than the other terms denoting decrease; *e.g.*, it is customary to say 10 c.c. or one-tenth of a c.c., instead of 1 decimeter and 1 millimeter. The term c.c. is also used, though incorrectly, when referring to volume measures of smaller amounts than the liter, but in the Pharmacopœia the term *milliliter* (the millimeter being the equivalent of one-tenth of a c.c.) and its abbreviation *mil* have been substituted for fractional quantities of a liter.

TABLES OF WEIGHTS AND MEASURES

METRIC

Weight	Written	Approximate equivalent
1 milligram (mg.)	0.001	1/65 grain
10 milligrams = 1 centigram (cg.)	0.01	1/6 grain
10 centigrams = 1 decigram (dg.)	0.1	1½ grains
10 decigrams = 1 gram (gm.)	1.0	15 grains
1000 grams = 1 kilogram (kilo.)	1000.0	2½ pounds
Volume		
1 cubic centimeter (c.c.) (1 c.c. of water weighs 1 gm.)	1.0	15 minims
1000 cubic centimeters = 1 liter (L)	1000.0	34 fluidounces
Length		
1 millimeter (mm.)		1/25 inch
10 millimeters = 1 centimeter (cm.)		⅖ inch
10 centimeters = 1 decimeter (dm.)		4 inches
10 decimeters = 1 meter (m.)		40 inches

Apothecaries

Weight (Troy Weight)

1 grain (gr.)	0.06 gm.
10 grains	0.6 gm.
20 grains = 1 scruple (℈)	1.3 gm.
3 scruples = 1 dram (ʒ)	4.0 gm.
8 drams = 1 ounce (℥)	30.0 gm.
12 ounces = 1 pound (lb.)	372.0 gm.

Volume

1 minim (m.)	0.06 c.c.
60 minims = 1 dram	4.0 c.c.
8 drams = 1 ounce	30.0 c.c.
16 ounces = 1 pint (O)	472.0 c.c.
2 pints = 1 quart (qt.)	950.0 c.c.
8 pints = 1 gallon (Cong.)	

Length

1 inch (in.)	2.5 cm.
12 inches = 1 foot	30.48 cm.

Exact Equivalents of Metric and Apothecaries' Weights and Measures According to the U. S. Pharmacopœia

Volume

1 c.c.	16.23 minims
1 liter (1000 c.c.)	33.8 ounces

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1 minim	0.061 c.c.
1 fluidram	3.696 c.c.
1 fluidounce	29.57 c.c.
1 pint	473.18 c.c.

Weight

1 milligram	0.0154 grain
1 centigram	0.1543 grain
1 gram	15.4324 grain

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1 grain	0.065 grams
15 grains	0.972 grams
1 dram	3.89 grams
1 ounce troy weight	31.1 grams
1 ounce avoirdupois weight	28.35 grams

Approximate Equivalent of Domestic, Metric and Apothecaries' Measures

1 teaspoonful	=	4 c.c.	=	1 dram
1 desertspoonful	=	8 c.c.	=	2 drams
1 tablespoonful	=	15 c.c.	=	4 drams
1 teacupful	=	120 c.c.	=	4 ounces
1 large cup	=	240 c.c.	=	8 ounces
1 tumbler	=	180–240 c.c.	=	6–8 ounces
1 sherry glass	=	30 c.c.	=	1 ounce
1 claret glass	=	120 c.c.	=	4 ounces
1 champagne glass	=	135 c.c.	=	4½ ounces

PERCENTAGE STRENGTH OF LIQUIDS

By per cent., it will be remembered, is meant parts in one hundred. In the preparation of drugs solids are weighed and liquids are measured, so that in making a 20 per cent. pharmaceutic solution 20 grams of the drug to be dissolved are mixed with enough solvent to make the total measure 100 c.c. Of such a solution, 100 c.c. will contain 20 grams of the drug. To make a one per cent. solution 1 gram of the drug would be used; for a 10 per cent., 10 grams; for a 15 per cent., 15 grams and so on, and in each case enough solvent is used to make the total measure 100 c.c.

To give one gram of a drug that is in a 1 per cent. solution will necessitate giving 100 c.c., while ½ gram will be represented by 50 c.c.; $\frac{1}{50}$ of a gram by 2 c.c. and $\frac{1}{100}$ of a gram by 1 c.c. Of a 2 per cent. solution, 50 c.c. will contain 1 gram; of a 3 per cent., 33 c.c.; of a 4 per cent., 25 c.c.

To find out how much of a drug to use to make larger quantities than 100 c.c. multiply the per cent. required by the number of hundred c.c. wanted; thus to make a liter (1000 c.c.) of a 5 per cent. solution, it will require 50 grams of a drug, because $5 \times 10 = 50$. To make 1500 c.c. of a five per cent. solution, it will require 75 grams, because $5 \times 15 = 75$. To make 2 liters (2000 c.c.) of a 2 per cent. solution, it will require 40 grams, because $2 \times 20 = 40$.

Means of Reckoning the Amount of Drug Required Using Apothecaries' Measure.—According to the apothecaries' measure, there are 480 minims or grains in an ounce, but, to facilitate reckoning, in the making of solutions, the ounce is generally considered as having 500 minims or grains and the pint 8000. Therefore, as 1 per cent. means 1 part in one hundred parts, whatever the system used, 5 minims or grains of a drug with enough solvent to make the total measure 500 minims will be required to make one ounce of a 5 per cent. solution. To calculate how much drug to use to make solutions of different percentages, multiply the required per cent. by 5 thus.

To make one ounce of a 2 per cent. solution, 10 grains are required.

To make one ounce of a 5 per cent. solution, 25 grains are required.

To make one ounce of a 10 per cent. solution, 50 grains are required.

TABLE SHOWING THE AMOUNT OF DRUG TO USE IN MAKING ONE PINT OF SOLUTION, THE PINT BEING CONSIDERED AS CONTAINING 8000 GRAINS, OR 500 GRAINS TO THE OUNCE

Per cent	Which is equivalent to	Amount of drug
½	1 part in 400	20 grains
¼	1 part in 200	40 grains
1	1 part in 100	80 grains
2	1 part in 50	160 grains
3	1 part in 33⅓	240 grains
4	1 part in 25	320 grains
5	1 part in 20	400 grains
10	1 part in 10	800 grains
20	1 part in 5	1600 grains
25	1 part in 4	2000 grains

In connection with solutions, it is necessary to differentiate between such terms as 1 in 20 and 1 to 20; the former term implies 1 part to 19, *e.g.*, 1 c.c. of carbolic and 19 c.c. of water, while the second term implies 1 part of solute[1] and 20 parts of solvent.[2] Bichlorid of mercury,

[1] The substance dissolved.

[2] The liquid used to dissolve the solute.

1–32, for example, would signify 1 part by weight of bichlorid of mercury in enough water or other solvent to make 32 parts by volume.

A method of estimating how much of a medicine to give when the preparation on hand contains a different fractional part of a grain of the drug from that ordered; e.g., the dose ordered is $\frac{1}{25}$ *of a grain of strychnine and the solution on hand is one in which* each 10 minims contains $\frac{1}{30}$ of a grain. To find out how much to give, multiply the denominator of the fraction of the amount of drug contained in the solution on hand by the number of minims containing it and divide the result by the denominator of the fraction of the amount of drug that is to be given. Thus: $30 \times 10 = 300 \div 25 = 12$. Therefore, 12 minims of a solution, of which each 10 minims contains $\frac{1}{30}$ of a grain of the drug, will contain $\frac{1}{25}$ of a grain of the drug.

For another example, the solution on hand contains $\frac{1}{30}$ of a grain in each 10 minims (*i.e.*, 10 minims = $\frac{1}{30}$ of a grain) and a dose of $\frac{1}{60}$ grain is wanted. Following the rule in the last example, $30 \times 10 = 300 \div 60 = 5$. Five minims of the solution will be required.

When necessary to give a different fractional part of a solid drug from the one at hand, it is usually better to dissolve the solid. Thus, if the strychnine in the first example were in solid form, two $\frac{1}{30}$ of a grain tablets could be dissolved in enough water to make 20 minims and, as in that example, 12 minims would give $\frac{1}{25}$ of a grain. If, in example two, the strychnine had been in solid form, one $\frac{1}{30}$ of a grain tablet could have been dissolved in enough water to make 10 minims and 5 minims of this used.

To estimate the amount to use in making a weaker from a stronger solution:

Divide the number of minims in the required amount of solution by the number representing the denominator of the weaker solution and multiply the result by the number representing the denominator of the stronger solution. Thus, to make a pint of 1–1000 ($\frac{1}{1000}$) bi-

chloride from a solution 1–32 ($\frac{1}{32}$), the pint being considered as containing 8000 minims:

$8000 \div 1000 = 8 \times 32 = 256$. 256 minims (4 drams, 16 minims) of bichlorid solution 1–32 will be required to make a solution 1–1000.

PRESCRIPTIONS

It is advisable for a nurse to be able to read a doctor's prescription and thus the ordinary prescription form and abbreviations commonly used are given here.

According to custom, a prescription is written in six parts, viz.:

1. The name of the patient and the date. The name is usually omitted, however when the prescription is for the treatment of a venereal disease or where it is best for esthetic reasons, as in prescribing a vaginal douche. Also, the pharmacist is expected to put the name on the label as this lessens the danger of his sending the wrong bottle or of mistakes if there is more than one patient in the family.
2. The symbol ℞ (pronounced R X) which is used as an abbreviation of the Latin word *recipe* which signifies *take thou.*
3. The name and quantity of each ingredient.
4. Direction to the pharmacist for compounding the drug, *i.e.*, whether he is to mix (M. or Misce) the ingredients, or make them into an emulsion. or into pills, etc., or put them into capsules.
5. The directions that the pharmacist is to place on the label. These are preceded by the symbol S or Sig., used as abbreviations of the Latin word *signa*, meaning *write* or *label.*
6. The physician's signature.

A typical form of an ordinary prescription is as follows:

For Mrs. Brown, March 24, 1920
℞. Bismuthi subnitratis..... ℥ii
Misturæ cretæ.....q.s. ad ℥iii
M. et Sig. ℥ii with a little water every three hours
B. B. Smith, M.D.

Interpreted, this would read: Take two drams of bismuth subnitrate and a sufficient quantity of chalk mixture to make the total measure three ounces, mix them together. Write on the label "Two teaspoonfuls with a little water every three hours."

ABBREVIATIONS AND SYMBOLS COMMONLY USED IN WRITING PRESCRIPTIONS AND ORDERS

Abbreviation	Derivation	Meaning
aa	ana	of each
A. c	ante cibum	before meals
Ad lib	ad libitum	as much as desired
Alt. dieb	alterius diebus	every other day
Alt. hor	alterius horis	every other hour
Alt. noc	alterius nocta	every other night
Aq. dest	aqua destillata	distilled water
Aq. pur	aqua pura	pure water
B. i. d	bis in die	twice a day
C	congius	a gallon
C		centigrade
Cum	cum	with
C. or c.c		cubic centimeter
Cap	capiat	let him take
Decub	decubitus	lying down
Dil	dilutus	dilute
F		Fahrenheit
F	fac	make
Fld	fluidus	fluid
Ft	fiat	let it be made
Ft	fiant	let them be made
Gm	gram	gram or grams
Gr	granum or grana	grain or grains
HCL	chemical symbol	hydrochloric acid
KI	chemical symbol	potassium iodide
Lb	libra	pound
Liq	liquor	liquid
M	misce, mistura	mix, mixture
M	minimum	a minim
NaCl	chemical symbol	sodium chlorid, *i.e.*, common table salt
O	octarius	a pint
O	ovum	egg
P.c	post cibum	after meals
P. r. n	pro re nata	as occasion arises

Abbreviation	Derivation	Meaning
Pulv	pulvis	a powder
Q. h	quaque hora	every hour
Q. s	quantum sufficit	as much as is sufficient
℞	recipe	take
S. or sig	signa	give the following directions
S. o. s	si opus sit	if necessary
Sp. gr		specific gravity
Ss	semi, semissis	one-half
T. i. d	ter in die	three times a day
Tinct.	tinctura	tincture
Ung	unguentum	ointment
μ	micron	the millionth part of a meter
ʒ	drachma	dram
℥	uncia	ounce
℈	scrupulum	a scruple

THE ACTION OF DRUGS

TERMS USED IN DESIGNATING THE SITE OF A DRUG'S ACTIONS

The actions of a drug at the site of its application (whether this be the skin, the alimentary tract, the respiratory tract, or the mucous membrane of other parts, or subcutaneous tissue) are spoken of as its *local actions*. **Actions produced after absorption** are termed *remote actions*, because they occur at a distance from the site of application, and *systemic actions*, because they only take place after the drug has been absorbed into the system. Some drugs are used for their local actions only, others for both local and systemic actions. Some drugs have no local action and, on the other hand, some drugs are not absorbed or else they are so much diluted after absorption that they have no remote actions.

The actions of a drug on tissue with which it comes in contact, whether before or after absorption, are spoken of as its *direct actions* while the effects that a drug produces on organs that it **does not act upon directly,** but influences through some other organ or system, are termed *indirect actions*. For example, a drug may indirectly influence practically every part of the body by its direct action on the heart or some part of the nervous system.

The activities which a drug induces by stimulating afferent nerve-endings are termed *reflex actions*.

When a drug acts only upon one or a few organs it is said to have a *selective action*, but **if it affects most of the tissues** of the body it is said to have a *general action* **and if this action tends to be harmful,** even though only in poisonous doses of the drug, the latter is called a *general protoplasmic poison*.

That many drugs affect certain tissues and not others is supposed to depend upon electrical attraction between

the drugs and some constituent of the protoplasm of the tissues they affect. Formerly, this attraction was spoken of as *chemical affinity*, but, it is now believed, the attraction that causes elements to unite and to remain together in a compound, as well as many other similar phenomena, depends upon electrical charge.

HOW DRUGS MAY ACT AS REMEDIES

Drugs may act as remedies by: (1) Destroying or removing some disturbing influence, *e.g.*, bacteria or their toxins; (2) providing some lacking body constituent (*e.g.*, hydrochloric acid, when the gastric glands are not manufacturing a sufficient supply; (3) changing the distribution of the fluids in the body, see under salt action; (4) changing abnormal reaction of body fluids; (5) softening or lubricating tissue with which they come in contact, by virtue of their own properties, and not by promoting any change in the tissue; (6) protecting the tissues from irritation by forming a coating on their surface or by absorbing irritating material; (7) causing some chemical or physical change[1] in the protoplasm of the organs they act upon and thereby inducing either stimulation, irritation or depression; (8) unknown means; for some time it was thought that such effects as stimulation and depression were practically always the result of some physical or chemical change in protoplasm, but investigation has not upheld this theory and it is now believed that some drugs alter the activities of cells in other ways, possibly, in some cases, by their presence, changing the electrical equilibrium or altering the adsorption properties of the tissue cells.

[1] A physical change, it will be remembered, is one in which the state of matter (solid, liquid or gaseous) is changed and a chemical change one in which the composition of matter is altered. An example of a physical change wrought by drugs is the liquefying, by ether and chloroform, of certain fat-like substances in the cerebral protoplasm to which the narcotic action of these drugs is partly due. An example of a chemical change is the coagulation of the protein of protoplasm by combining with it and forming a new compound.

SOME TYPICAL ACTIONS OF DRUGS

Astringent Action.—This is produced chiefly on mucous membranes and raw tissues and implies shrinking or contraction of the affected tissues and usually involves lessening of secretion and, sometimes, of the sensitiveness of nerve-endings in the area. Drugs will act as astringents by: (1) Contracting the arterioles in the part, thus diminishing the amount of blood in the vessels; (2) extracting water from the superficial cells; (3) coagulating the protein in the outer cells. If astringents are used in concentrated form they will cause irritation and those which coagulate protein will cause inflammation and even destroy tissue.

Salt Action.—This implies (1) the effects that many substances, such as the mineral salts, sugar, urea, and other solids that can circulate in the blood in sufficient quantity, have upon osmosis. It will be remembered that osmosis signifies the passage of fluid through a membrane and that, if two solutions of unequal density are divided by a permeable membrane, the less concentrated one will pass through the membrane more rapidly than the other until the solutions on both sides of the membrane are of equal concentration. For example, if the concentration of the blood is raised by the injection, or the absorption, of a hypertonic[1] salt solution, a greater amount of fluid than usual will pass from the tissues into the blood and the transudation of fluid from the blood into the tissues will be less than usual until the blood and the fluid in the tissues (*tissue lymph*) are of equal density. (2) The term salt action is also used to express the tendency common to many soluble substances in the body, as elsewhere, to diffuse (spread out) until they are equally distributed in a part. For example, if the lymph surrounding the cells contains more sugar and less salt than the fluid within the cells there will be a passage of sugar into the cells and

[1] Salt solutions of the same concentration as the blood are said to be isotonic with the blood, those with a greater concentration (*i.e.*, containing a larger amount of solid matter) are termed hypertonic and those of lesser density, hypotonic.

of salt from the cells until the fluids within and without the cells have about the same composition. As any considerable change in the constituents of the intracellular fluid will affect the activities of the cells, a lack of normal diffusible substances in the tissue lymph (which comes from the blood) or their presence in excess, or the addition of unusual ones, may affect the cells, even though the substances are themselves inactive, *i.e.*, they cause no change in the chemical or physical constituents of the cell protoplasm.

Stimulation.—By this is meant to excite to functional activity; for example, when receptors are stimulated they transmit impulses to nerve-centers; when nerve-centers are stimulated they send out impulses to the muscles or glands which they control; when glands are stimulated they secrete; when muscles are stimulated, they contract, and all cells probably respond to stimulation by increasing the chemical activities upon which their metabolism depends. Irritation is a common cause of stimulation, but a number of non-irritant drugs also stimulate different organs, especially the heart and parts of the nervous system. How they do so is not known. Poisonous doses of non-irritant stimulants may cause death by over-stimulating some vital organ, because overstimulation results in depression, but such drugs do not permanently injure the tissues they affect and, if the patient can be kept alive until the poison is eliminated and the depressed cells have time to rest and assimilate material for their repair, there will be no permanent harmful after-effects.

Irritation is a term often used as a synonym for stimulation, but this is incorrect, because though, as stated in the preceding paragraph, irritation induces stimulation, stimulation is not dependent upon irritation and severe irritation induces inflammation and even corrosion of tissue and, when the injury is severe, leaves permanent lesions similar to the scar tissues which form in wounds due to other causes. The local reaction which follows irritation is one

of nature's ways of protecting the body from harmful substances and consists in increased secretion, if there be glands in the part, dilation of the local blood-vessels and the consequent inflow of a larger amount of blood and exudation of fluid from the blood-vessels into the tissues. Such a reaction, it can be appreciated, supplies fluid to wash away or dilute the irritant, extra phagocytes to fight or carry it away, if necessary, and extra nutritive material to repair any damage done. Such a reaction is also of value to physiological processes such as digestion, and to those which occur on the repair of wounds and of some other abnormal conditions of tissue. The presence of an irritant also stimulates sensory nerve-endings in the part. The result of this on the skin is described under Counter-irritants and the results in the alimentary canal under Carminatives, Cathartics and Emetics. Most of the drugs which act as irritants do so by promoting some change in the protoplasm of the affected cells, such as extracting water or fat or coagulating protein, but the cause of irritation by some drugs is unknown.

Depression is the opposite of stimulation and implies lessened activity or, if intense, paralysis or inability to function. The reason for the depressant action of some drugs is unknown. It is associated in some cases with change in the protoplasm; also, depression follows over-stimulation of the affected organs; in such case the conditions produced are thought to be similar to those induced by ordinary fatigue, but very much intensified.

Other terms in common use to describe drug actions are as follows:

Antagonistic Action.—This implies that the drugs in question interfere with the action of each other. They may do so by producing opposing effects on the same organ or upon different organs; for example, if one drug stimulates the cardiac accelerator center and the other depresses the heart muscle very little effect will be obtained from either drug, unless the action of one is stronger than that of the other.

Synergistic Action or Synergism.—These terms are used when drugs with similar actions help one another. For example, certain cathartics when used together will act better than when used alone, this is true also of some narcotics and analgesics. It is thought that, synergists, at least in some cases, may act upon different parts of the organs they affect.

Therapeutic Action.—This term is generally used to signify the effects of a drug that are of value in the cure of the symptoms that the drug is used to alleviate.

Physiologic or Physiological Action.—When applied to drugs, these words generally indicate all the effects of a drug, whether they are curative or not.

Pharmacologic Action.—This signifies what is known of the action of a drug and thus it has practically the same significance as physiologic action.

Cumulative Action.—This is a term used for the propensity of certain drugs to accumulate in the system. Accumulation is generally the result of slow elimination of the drug. **The drugs most likely to accumulate in the system are:** Digitalis, arsenic, mercury, lead and silver.

CLASSIFICATION OF DRUGS ACCORDING TO THEIR EFFECTS

Drugs are sometimes classified according to their most pronounced effects. The important classes needing any explanation are as follows:

Absorbents—substances used to absorb excessive secretions, bacterial toxins, and gas.

Abortifacients—agents which produce abortion. Any drug which contracts the uterine muscle or changes the circulation in the uterus, if taken during pregnancy, may cause abortion.

Alteratives—drugs which produce favorable changes in the processes of nutrition and repair. The class includes all drugs which aid metabolism.

Anesthetics—remedies that induce insensibility to pain. They are classed as **general anesthetics and local anesthetics.** The former being those which depress nerve-centers and

induce general insensibility and unconsciousness and the latter those which depress sensory nerve-endings with which they come in contact and induce local anesthesia.

Analgesics and anodynes—remedies that relieve pain, but do not produce the degree of insensibility caused by anesthetics. The term analgesic is applied to drugs which act after absorption and their effect is generally the result of depression of sensory areas in the brain or of relay centers leading to those areas. The term anodyne is used more especially for external applications that relieve pain by their local action.

Anhydrotics—drugs which check the secretion of sweat. Most of the drugs do so act by depressing the nerve-endings in the sweat glands.

Antacids—substances that neutralize acids. They may be used (1) to act upon the gastric juice, or, after absorption, (2) to overcome systemic acidosis, or (3) to lessen the acidity of the urine.

Anthelmintics include vermicides and vermifuges.

Antiemetics—remedies which check vomiting. As vomiting is induced in many ways, drugs with different actions are used as antiemetics; *e.g.*, antacids, to check irritation due to hyperacidity of the gastric juice; carminatives, see page 53, counterirritants; protectives, see page 60, remedies such as ice and local anesthetics which lessen the sensitiveness of nerve-endings in the stomach; analgesics.

Antiarthritics—drugs which relieve conditions present in gout.

Antiperiodics—drugs which prevent the periodic recurrence of symptoms such as the chill in malaria.

Antipyretics—remedies that reduce fever. Many drugs that reduce the temperature in fever will not, except in excessive doses have any effect upon it when normal. This is because the thermotaxic or heat-regulating centers are stimulated by changes in the blood temperature and, if anything occurs to increase heat loss, they induce the stimulation of the oxidative processes of the body and thus increase heat production. On the other hand, if oxidation

is increased as, for example, during exercise, chills, or convulsions, the thermotaxic centers stimulate the mechanisms causing loss of heat. Heat loss is due chiefly to the radiation of heat from the blood in the skin and the evaporation of perspiration and thus is increased by dilation of the skin vessels and diaphoresis. When there is fever, it is believed, the thermotaxic centers are depressed, usually by toxins that have been formed in the body, and thus only respond to temperatures higher than normal. Drugs that act as antipyretics do so either by stimulating the centers, or by protecting them from the influence of toxins, or by direct action upon centers or nerve-endings that promote the dilations of the skin blood-vessels or those which induce perspiration. The chief cause of heat production in the body is the oxidation of material derived from food, but hormones formed by the ductless glands are essential for the process and the rate of oxidation depends upon the degree of muscular contraction, and muscular contraction upon nerve-impulses. Therefore, any drug which inhibits the activity of the hormones concerned with metabolism, or that depresses the nervous system will tend to reduce the temperature. Drugs with these actions are not used intentionally as antipyretics, but a few used for other purposes have such effects.

Antiseptics—substances which inhibit the growth and activity of bacteria.

Antisialogogues—drugs which check the secretion of saliva. This is usually the result of depression of the secretory nerve-endings in the salivary glands.

Antispasmodics—drugs which tend to overcome muscular spasms and convulsions. This effect may be produced by depression of nerve-centers or of motor nerve-endings, or of muscle tissue.

Aperients—mild cathartics.

Astringents—described page 47.

Bitters—drugs with a bitter taste that, by stimulating the taste buds, increase the flow of saliva and gastric juice and improve the appetite and in this way aid digestion.

Carminatives—drugs which by their local action on the alimentary canal cause the expulsion of gas from the stomach and intestines. Some drugs do this by increasing the peristaltic action of the intestines and others by overcoming spasmodic contractions. The drugs having carminative action also stimulate the olfactory nerve-endings and thereby increase the secretion of saliva and gastric juice. Also, they irritate the membrane of the alimentary canal and thus increase the amount of blood in the membrane and, by stimulating afferent nerve-endings, they cause a transitory stimulation of important medullary centers, viz., the vasoconstrictor, cardiac accelerator, and respiratory centers. Thus they tend to cause a temporary rise of blood-pressure which may improve the circulation in the brain sufficiently to overcome faintness.

Cathartics—agents which promote the evacuation of the bowels. This is commonly brought about either by increasing the bulk of the intestinal contents, by irritating the intestinal membrane, or by stimulating the contraction of the muscle tissue of the intestines, either directly or by stimulating the part of the vagus nerve supplying the intestines.

Caustics or escharotics—agents which destroy tissue.

Cholagogues—drugs which increase the flow of bile. Formerly the drugs which have this effect were thought to stimulate the liver cells to secrete bile, but it is now considered that, with a very few exceptions, the increased excretion of bile depends upon the contraction of the muscle tissue in the bile ducts which forces out the stored bile

Circulatory stimulants—remedies which improve the circulation.

As one of the most common and important uses of drugs is to overcome conditions interfering with the circulation it will be well to recall those which are essential for normal circulation; viz.: (1) The heart must be contracting properly; (2) the caliber of the blood-vessels and (3) the amount and condition of the blood must be normal. In order that the heart may contract properly,

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the following properties of its muscle must be normal: (1) Irritability, *i.e.*, its sensitiveness or readiness to respond to stimuli—if its irritability is below par the muscle will not react well to stimuli, if irritability is excessive, what is known as *fibrillation* may occur, *i.e.*, all the muscle fibers will not contract equally and at the same time; (2) tonicity, *i.e.*, the state of partial contraction persisting even during diastole, which prepares the heart to respond to stimuli and prevents it being dilated while it is not in active contraction by the blood pouring into it from the large veins; (3) contractility, or the power to contract and force the blood onward; (4) conductivity or the transmission of nerve impulses from the sinus node (where they discharge into the heart) over the entire organ. It will be remembered that the rhythmic contraction (systole) and relaxing (diastole) of the heart muscle is maintained by the salts of the blood, especially the sodium and potassium salts, which cause contraction, and those of calcium, which cause relaxation, but the rate and strength of its action is regulated by impulses coming over the cardiac accelerator and vagus nerves, the former increasing the rate and strengthening the contraction and those from the vagus inhibiting the results of the accelerator impulses and preventing excessive rate and contraction. The nerve-fibers enter the heart at what is known as the *sinus node* or the *pacemaker*, which is in the region where the large veins enter the right auricle. The impulses pass from here over the fibers of the auricles and are transmitted to the ventricles over minute bundles of muscle fibers, known as the *bundles of His* or the *auriculo-ventricular bundles*. Over-doses of certain drugs and disease of the heart may so reduce the property of conductivity as to interfere with the passage of impulses over these bundles and create a condition known as *heart-block* in which the ventricles act only in response to the salts of the blood and, not being controlled by nerve impulses, beat at a rate of 30 to 40 beats per minute, even when the auricles are acting unusually rapidly. As the pulse in the arteries results from the ventricular contraction, its rate will be that of the ventricles.

The accelerator mechanism is stimulated by all conditions calling for an increased amount of nutrient and oxygen in the tissues (*e.g.*, exercise and fever), by stimuli that affect the sympathetic system, and by certain drugs, and the resulting impulses strengthen the contractions of the heart muscle and also increase the rate of its action, chiefly by lessening the time of diastole, *i.e.*, relaxation. As it is during diastole that the heart muscle gets its supply of nutrient oxygen, etc., the coronary vessels being emptied during systole (contraction) if the rate of the heart continues fast for any length of time, as in fever, its contractions (and consequently the pulse) will become weak, though the latter may remain rapid, but

the increased rate is no longer a sign of stimulation. Under such circumstances a drug which stimulates the cardiac accelerator mechanism, especially if it also stimulates the heart muscle or increases the contraction of the blood-vessels, may, by forcing the heart to take stronger contractions, slow the rate.

When the heart's action is abnormally rapid, a drug which stimulates the vagus, by slowing the rate and thus allowing the heart to get more nourishment, etc., may act as a stimulus, though, ordinarily, stimulation of the vagus tends to weaken the heart's action by prolonging and intensifying relaxation and lessening the irritability and conductivity of the heart muscle. It will be noticed in the study of the drugs that some of the most important circulatory stimulants stimulate both the vagus and the heart muscle and, by the latter action, they tend to overcome the bad effects of the vagus stimulation, for a true stimulant of cardiac muscle will increase its irritability, tonicity and contractility.

The normal caliber of the blood-vessels is maintained by some unknown intrinsic property of their muscle tissue and by nerve impulses. With the exception of the vessels in the brain, lungs and heart, the motor nerve supply of the vessels is controlled by the vasoconstrictor centers. The centers controlling the vessels in different parts, as the skin, muscles, and abdominal viscera are not usually affected by the same stimuli, at any rate to the same extent, and thus a drug that causes contraction of the vessels in the abdominal viscera (the splanchnic vessels) increases the amount of blood in the brain, lungs and heart and, though to a lesser degree, in the skin, muscles and kidneys. Conditions which depress the heart action, either by their influence on the vaso-constrictor mechanism or the tissues of the blood-vessels, also tend to cause relaxation of the vessels with a consequent low blood-pressure and this further interferes with the heart's action, because, the heart needs a certain amount of resistance. Therefore, when the blood pressure is abnormally low, a drug that stimulates the vasoconstrictor mechanism will improve the heart's action, even though it does not directly affect the heart or its nerve supply. Blood pressure rarely becomes dangerously high, except in some abnormal conditions of the heart, kidneys or blood-vessels, because of the depressor nerve (an afferent branch of the vagus) which is stimulated when the blood pressure rises above normal and then transmits impulses to the vasoconstrictor center and lessens its activity. However, in diseases of the organs just mentioned blood pressure may be abnormally increased and then drugs which relax the vessels may be prescribed. Blood-vessels may be relaxed by depressing their muscle tissue, or by depressing some part of the vasoconstrictor mechanism or, presumably, in some cases, by stimulating vasodilator nerves; but

only the vessels in a few parts of the body have been proven to have dilator nerves and the cause of vasodilation in many cases is unknown, especially vasodilation due to irritation and physiological activity. It is thought, however, that irritation produces activity and activity from any cause results in the decomposition of material in the tissues thus giving rise to chemical substances that, it is believed, either by direct effect upon the tissue of the blood-vessels or, indirectly, by influencing nerve-endings, cause the vessels in the part to become relaxed. Temporary localized relaxing of blood-vessels, when those of other parts are in a state of normal contraction, will cause the area to become warm and red and, if there are glands in the part, it will favor secretion.

Change in the volume of blood, except as a very transitory condition is nearly always a decrease because, if an unusual amount of liquid is injected or absorbed into the blood-vessels, the kidneys and, sometimes, the sweat glands are stimulated and quickly get rid of the excess, also there may be increased osmosis into the tissues. A decrease in the amount of blood circulating in the vessels may be due to (1) general dilation of the blood-vessels, in which case there will be an abnormal amount in the abdominal vessels; (2) excessive loss of fluid from the body as by hemorrhage, purging, vomiting and diaphoresis. A slight loss will soon be made good as far as the blood is concerned, because its concentration will be raised and this will induce osmosis of fluid from the tissues as explained under salt action. However, unless there is an excessive amount of fluid in the tissues, as in dropsy, the removal of fluid will be injurious to the tissue cells and, consequently, the loss must be made good as quickly as possible.

To summarize the ways in which remedies may improve the circulation: By; (1) directly stimulating the heart muscle; (2) stimulating some part of the cardic accelerator mechanism; (3)depressing some part of the vagus mechanism, which has the same effect as stimulating the accelerator; (4) stimulating the vagus when the pulse is excessively rapid; (5) improving the circulation in the coronary vessels and, thereby, the nutrition of the heart muscle; (6) stimulating some part of the vasoconstrictor mechanism; (8) relaxing the blood-vessels when blood-pressure is abnormally high; (9) increasing the amount of blood by transfusion, etc., when the amount in circulation is depleted either as the result of loss of blood or its fluid or of relaxed vessels.

Counterirritants—agents which, by irritating the skin, counter or relieve irritation or pain in viscera and muscles. Theories regarding the reasons for their effects are given in the section on Volatile Oils.

Cycloplegics—drugs which paralyze the ciliary muscles of the eyes and thus prevent accommodation for viewing objects near at hand.

Demulcents—mucilaginous or bland substances which lubricate and coat a surface and thus protect it from irritation.

Depilatories—agents that remove hair.

Detergents—cleansing agents.

Diaphoretics—agents which increase the secretion of sweat. Drugs may increase this secretion either by stimulating the heat regulating center, or the sweat centers, or the secretory nerve-endings in the sweat glands; also, drugs which increase the amount of blood in the skin, and thus around the sweat glands, favor diaphoresis, but the secretion of sweat is not as much influenced by the amount of blood present as are the secretions of other glands. Other means employed to induce diaphoresis are (1) active exercise which increases heat production; (2) the use of heavy covers or clothing, which inhibits loss of heat; (3) surrounding the body with heat. The more common therapeutic uses of diaphoretics are: (1) In edema, to raise the concentration of the blood (by removal of fluid) and thus favor the absorption of the excess fluid in the tissues; (2) when the kidneys are not functioning properly, to remove some of the salts and nitrogenous matter usually eliminated through those organs; (3) to relieve internal congestion that favors the activity of bacteria which cause "colds;" (4) to lessen obesity (depriving the body of water favors the oxidation of fat); (5) to reduce temperature.

Digestants or **digestives**—agents that aid digestion. The drugs of this class act either by stimulating the digestive juices or they themselves contain ferments which aid digestion.

Disinfectants—agents that destroy germs.

Diuretics—agents which cause diuresis, *i.e.*, increased secretion of urine. The kidneys are not furnished with secretory nerves and, therefore, diuresis is caused either by (1) direct non-irritant stimulation of the kidney cells; (2) irritation of the kidneys; (3) increasing the blood pressure in the renal vessels. The latter effect may be induced by: (1) Improving the circulation; (2) contracting the blood-vessels in the other abdominal viscera and, thereby, forcing more blood into the renal vessels; (3) increasing the amount of fluid in the blood. The amount of fluid in the blood may be augmented either by (*a*) increasing the intake of fluid or (*b*) by using substances, such as mineral salts and urea, that raise the osmotic pressure of the blood and thereby promote the osmosis of fluid from the tissues into the blood, as described under Salt Action. A large number of drugs used for other therapeutic purposes cause diuresis and in most cases the diuresis has no influence upon the effects for which the drug is used but it is important to remember that almost all irritant drugs during elimination irritate the kidneys and, in toxic doses, they will not only cause diuresis, but injure the kidney cells and, both for this reason and because of the loss of water from the body, the diuresis is likely to be followed by anuria and, if the cells are badly injured, there will be albumin and casts and, sometimes, blood in the urine. To lessen the danger of these conditions, water must be given freely in the treatment of poisoning by irritant drugs.

Drastics—cathartics which induce excessive purging and griping.

Ecbolics—drugs which produce contractions of the uterus. They may do so either by stimulating the muscle tissue of the uterus or by stimulating the sympathetic nervous system.

Emetics—drugs used to produce emesis or vomiting. Vomiting results from many causes, but the drugs used purposely to produce emesis do so either by irritating the

stomach or by stimulating the vomiting center in the medulla. Those which act in the former manner are classed as *reflex* or *indirect emetics* and those which stimulate the center, as *central* or *direct emetics*.

Emmenagogues—agents which bring on the menstrual flow. Drugs used for this purpose are either tonics which improve the general health, including the condition and the circulation of the blood; drugs which cause contraction of the uterine muscle; drugs which increase the amount of blood in the uterus, as described under the Volatile Oils and the Drastics Cathartics.

Emollients—fatty substances used to soften and protect the skin and wounded surfaces.

Epispastics or **vesicants**—irritants used to induce blisters.

Escharotics—agents which destroy tissue.

Expectorants—substances used to facilitate the expectoration of bronchial mucus. This effect is usually produced by increasing the secretion of mucus and saliva and such stimulation is generally the result of reflexes induced by stimulating nerve-endings in the mouth or by a nauseant (irritant action) in the stomach. Mucus secreted under such stimulation is generally thin and watery and helps to wash off the tenacious mucus. Also irritant drugs which promote coughing and those which improve the tone of the bronchial muscle will aid in the expulsion of mucus. Drugs may act directly upon their administration or (when they are eliminated through the bronchial membrane) during excretion. Alkalies put into a test-tube with mucus will liquefy the latter and, for this reason, were much used in expectorant mixtures, but is now thought doubtful if they come into sufficient contact with the mucus to be of value, except when they are used in throat and nasal douches. Drugs which lessen the secretion of mucus are sometimes classed as *sedative expectorants*.

Galactagogues—agents which increase the secretion of milk. Drugs are rarely used for this purpose.

Hematinics—drugs which increase the amount of hemoglobin in the blood.

Hypnotics—drugs which induce a condition resembling sleep.

Hydragogues—cathartics which cause watery stools.

Laxatives—mild cathartics.

Lubricants—oily substances which lubricate, soften, soothe and protect surfaces from irritation.

Mydriatics—drugs which dilate the pupils of the eyes. This action may be induced by depressing the muscle tissue of the iris; by depressing some part of the portion of the third nerve supplying the circular muscle of the iris; by stimulating the sympathetic nerve supplying the radial muscle of the iris. In addition to dilating the pupils, mydriatics are likely to increase intraocular tension (*i.e.*, the tension of the fluid within the eyeball). They do so because excess fluid escapes from the eyeballs through minute lymph-channels which open at the margin of the pupil and when the latter is dilated the channels are more or less blocked.

Miotics—drugs which contract the pupils. Their action is generally caused by stimulation of the portion of the third nerve supplying the circular muscle of the iris.

Prophylactics—remedies used to prevent disease.

Protectives—substances used to protect the skin, wounds and mucous membranes. This class includes absorbents, collodions, demulcents, emolients, and lubricants.

Purgatives—cathartics which produce free evacuation of the bowels, but are not drastic.

Rubefacients—mild counterirritants.

Soporifics—same as hypnotics.

Stomachics—drugs which aid digestion. They may do this by stimulating the taste-buds and olfactory nerve-endings and thus inducing a reflex flow of saliva and gastric juice and by slightly irritating the mucous membrane of the stomach and thus increasing the amount of

blood in the membrane and inducing reflexes which increase the motor and secretory activities of the stomach.

Specifics—drugs which cure a disease by acting directly upon the germ or special condition to which the malady is due.

Styptics—drugs which check local hemorrhage.

Teniacides—drugs which destroy tape worms.

Tonics—remedies which increase the health and tone of the body. They may do this in several ways, as, for example, by improving the appetite and digestion; by improving the circulation; by increasing the amount of hemoglobin in the body; by stimulating the tissue cells and thereby the chemical activities upon which their nutrition depends; by stimulating the endocrine glands which control metabolism; by stimulating the nervous system and thus increasing muscle tone and the activity of the various organs.

Vermicides—drugs which destroy worms.

Vermifuges—drugs which expel worms.

Vesicants—drugs which produce blisters.

TOXICOLOGY

As previously stated, **Toxicology** is the science or study of poisons. **A poison has been defined as** *any substance that in small amounts will cause death or seriously injure the health.* Poisoning by drugs may be the result of criminal or suicidal intent or accident.

The symptoms of poisoning by drugs with actions that are at all similar are very alike and also the treatment for poisoning, therefore the study of the toxicology of the individual drugs will be very much facilitated if the following facts are remembered:

The majority of drug poisons can be classified as follows:

Irritants—these include corrosives, which destroy tissue and simple irritants, which cause inflammation, but not corrosion.

Nerve poisons or *neurotics*—these include nerve stimulants of convulsants, which cause spasms and convulsions, and nerve depressants or somnifacients, which induce sleep and coma.

Cardiac poisons, those which cause death by paralyzing the action of the heart.

Blood poisons, those which alter the hemoglobin or the corpuscles or interfere with the coagulable property of the blood.

Whatever the cause of poisoning one of the most dangerous conditions induced is that known as collapse, in which there is a deficiency of blood in the general circulation. This deficiency can be due to many causes some of which are very imperfectly understood. Examples are: Loss of blood or of fluid from the blood by continued vomiting and purging; dilation of the splanchnic arteries, or dilation of the capillaries. **The arterioles may become dilated as the result** of direct depression of their muscle tissue, or of their nerve-supply and the nerve

depression may be brought about by depressant drugs or by over-stimulation; for any intense stimulation of nervous mechanisms is likely to be followed by their depression. **Dilation of the capillaries** is thought to be brought about by chemical substances that are produced when tissue is injured and, when absorbed by the blood and carried through the body, depress the tissue of the capillary walls. Whatever the cause of the condition, the circulation of the blood is interfered with and the brain, lungs, and heart may not get enough blood to enable them to carry on their functions and then death ensues.

The symptoms of collapse depend upon the severity of the condition. In a mild form, there will be dizziness, faintness, a slight increase in the rate, and decrease in the strength of the pulse, and there may be nausea and vomiting, and the individual may faint. In severe collapse, the pulse becomes exceedingly weak and very rapid, except when the poison directly depresses the heart muscle, in which case, the pulse may be slow, though excessively weak; the skin becomes cold and clammy and covered with perspiration; it is usually cyanotic, except in poisoning by chloroform, when it is pale; the muscles are relaxed and weak; the temperature falls; the breathing becomes labored, slow, shallow, and inefficient, which causes a condition of partial asphyxia and, as the result of this, convulsions may occur.

Death from poisoning by drugs is very frequently due to cessation of breathing, for this may result from several causes, the more common ones being: (1) Direct depression of the respiratory center, which prevents it being stimulated by the carbon dioxid in the blood, this may be the result of depressant drugs or of fatigue from over-stimulation; (2) interference with the circulation which prevents sufficient blood reaching the center to promote its stimulation; (3) interference with the action of the muscles concerned with breathing either as the result of their paralysis or of their spasmodic contractions during convulsions.

In poisoning by most nerve depressants the typical symptoms are those of collapse with profound stupor. **In poisoning by nerve stimulants,** twitching of the muscles and convulsions will precede the depression. **In poisoning by irritants,** in addition to the symptoms of collapse, there will be the local ones caused by the irritation, these, if the drug has been taken by mouth, as is usually the case, will be vomiting, diarrhea, abdominal pain; the vomitus and feces are likely to contain mucus and blood and, when the drug is corrosive, shreds of membrane. Also, as more or less of all irritant drugs are eliminated through the kidneys, there is likely to be diuresis, followed, in some cases, by anuria or suppression, and, due to injury of the kidney cells, the urine may contain blood and casts and, if the cells do not function properly, albumin. Convulsions may occur as the result of the excessive reflex nervous irritation caused by the local injury and, possibly, due to the action of the drug on nerve centers after absorption. **In poisoning by drugs which cause changes in the hemoglobin,** asphyxia will be pronounced and will be shown by extreme dyspnea and cyanosis and convulsions. Many drugs with various actions cause skin rashes in overdoses. The causes of this, in some cases, are not known but irritant drugs that are eliminated in the perspiration and those which cause changes in the circulation of the blood in the skin are particularly likely to do so.

Treatment.—Poisoning by certain drugs requires special treatment and this is mentioned in the sections devoted to the description of such drugs, but certain principles are applicable to the treatment of poisoning by nearly all drugs. These are: (1) Prompt action is necessary, in some cases chiefly to prevent the local effects of the drugs and, in others to inhibit absorption. (2) The poison is removed if possible. (3) A chemical antidote is used if there is one and the substances formed by the interaction of the antidote and the poison washed away. (4) Physiological antidotes are employed. (4) Irritant drugs are

diluted and, as a rule, this is one of the first things to be done in the treatment of poisoning by irritants.

The measures used for the removal of the poison depend upon the way in which the drug has been taken. If it has been administered hypodermically its removal is difficult but if the mistake is noticed at once, cupping may have some result and, if a ligature is applied tightly around the limb above the point of administration, the absorption of the drug may be delayed sufficiently to allow a portion of the dose to be excreted before the whole amount has been taken up by the blood. Means must be taken at once to hasten excretion as described later. The removal of poisons from the skin, wounds, and accessible body cavities is affected by irrigations or lavage and from the stomach, in some cases, also by inducing vomiting. As soon as the treatment for the acute conditions have been attended to, measures are taken to hasten the removal of the drug through the excretory organs by giving a purgative and a diuretic and, if urine is not voided, catheterizing the bladder. In the case of drugs that, after absorption, are excreted into the alimentary canal a purgative is given even when the drug has been administered by hypodermic. Irritant cathartics and diuretics should not be used, especially in the treatment of poisoning by irritant drugs. An important point to bear in mind in the treatment of poisoning by irritant drugs is that the alimentary canal and kidneys are seriously inflamed by the poisons and, if the latter is corrosive, the stomach especially may be so corroded that the organ can be easily ruptured. For this reason, emetics, which would add to the irritation, are not used for the removal of irritants and lavage must be performed with exceedingly great caution, *i.e.*, the tube must be very thoroughly lubricated, it must be inserted without force, and the solution must be poured in slowly and the stomach must not be overdistended; it is better under such circumstances to siphon off the fluid as soon as a small quantity has been introduced, but to continue the lavage for some time.

When possible, the fluid used is a chemical antidote. When extensive corrosion of the stomach is feared it is better not to give lavage, but to depend upon the dilution and neutralization of the drug.

The substances used for diluting irritant drugs are milk; raw eggs only very slightly beaten; boiled starch water or other demulcent solution; but, if these are not at hand, water must be used; the physician frequently prescribes oils, but it is better for nurses not to give oil without a prescription, for oil increases the solubility of a number of drugs and thus hastens their absorption.

Emetics are not used in the treatment of poisoning by irritants; nor in advanced stages of strychnine poisoning; nor by depressants after symptoms of collapse are evident; for, in such case, the drug must have been absorbed, and an emetic is likely to increase the harmful effects of the drug. Emetics in common use are: Apomorphine, given by hypodermic; ipecac; copper sulphate; zinc sulphate; and mustard.

Chemical antidotes are substances that will combine with the poison to form a relatively harmless substance. The majority of antidotes act either by neutralizing, precipitating or oxidizing the poison.

For poisoning by acids, weak alkalies, such as magnesia oxid are used; this is discussed in the section devoted to acids; **for alkalies,** weak acids, such as vinegar and lemon juice are used. Acids and alkalies neutralize each other.

For metal salts, especially those of mercury, albumin, usually in the form of milk or raw eggs, is used.

For alkaloids, oxidizing agents such as hydrogen peroxid or, preferably, potassium permanganate[1] may be used or else substances which precipitate the alkaloids; these are iodine and tannin. For convenience, the latter is generally used in the form of strong boiled tea. It is not of much use for morphine, cocaine, atropine and aconite.

[1] These substances hold oxygen in loose combination and this unites with the poison and decomposes it. The dosage for this and the other drugs will be found in the sections describing them.

For glucosides, oxidizing agents, especially potassium permanganate.

Special antidotes used for certain drugs will be found in the sections describing the actions and uses of the drugs.

An important point to remember is that in many cases the compounds formed with the antidotes are not stable nor entirely harmless and thus they should be removed by lavage.

The physiological antidotes for poisons include everything that combats the symptoms or physiological effects produced by the poison. Examples are: (1) The treatment for collapse; (2) artificial respiration and other means taken to stimulate breathing; (3) the use of alkaline salts, usually given intravenously, to counteract systemic acidosis; this is described on page 241; (4) drugs and other means taken to arouse the patient in poisoning by nerve depressants; (5) nerve sedatives used to lessen nervous irritability in poisoning by nerve-stimulants; (6) demulcents and emollients used to soothe and lubricate irritated tissue in poisoning by irritants.

The usual treatment to prevent and overcome collapse is: 1. Keep the patient quiet, in order to give the heart as little work to do as possible. An exception to this rule will be seen in the treatment for poisoning by opium and its alkaloids.

2. Keep the patient warm. To do so, it is usually necessary to put hot water-bags in the bed and, if possible to give hot drinks and sometimes hot enemata. External heat is usually very important, because except when the patient has convulsions, the temperature is likely to become very much reduced for (1) the diaphoresis (excessive perspiration) increases the loss of heat while the weak circulation, by lessening the amount of oxygen taken to the tissues, and the muscular relaxation, tend to lessen the production of heat.

3. If the collapse is at all severe the patient's head should be lowered so as to favor the flow of the blood to

the brain. This is generally done by raising the foot of the bed.

4. The doctor is likely to give a blood transfusion or an intravenous infusion of a salt solution containing adrenaline and he may prescribe inhalations of oxygen, or the administration of camphor, strychnine, caffeine, atropine or pituitrin by hypodermic. It is always better for nurses not to give drugs without a doctor's order, except in extreme urgency, and, when the collapse follows over-stimulation of the nervous system, they should not give nerve stimulants such as caffeine, camphor, and strychnine.

The usual means taken to avert cessation of breathing are: Artificial respiration, inhalations of carbon dioxid with oxygen, stretching the rectum (which gives rise to reflexes), hot strong coffee is generally given by rectum, and caffeine and atropine by hypodermic.

To Summarize.—In the treatment of poisoning by all toxic drugs means must be taken to prevent collapse and the breathing must be watched and if its rate becomes much reduced (15 to 12 breaths per minute) means must be taken to prevent its cessation. If possible the drug is to be washed away; this, when it has been taken by mouth, is done by lavaging the stomach; if, however, the poison is a concentrated corrosive, it may be better to omit the lavage. When the implements for lavage[1] cannot be obtained at once, emetics are used, except in case of poisoning by concentrated irritants, and in advanced stages of poisoning by strychnine and depressants. If possible a chemical antidote is given, and the lavage repeated. Means are taken to hasten the excretion of the drug; these consist in giving all the fluid possible, a quickly acting, but non-irritant cathartic, and, sometimes, a non-irritant diuretic, and if the patient does not void urine, catheteriz-

[1] If a stomach tube cannot be obtained, ordinary soft rubber tubing of similar caliber to the stomach can be used after the end to be inserted has been made smooth; this can be done by holding it in a flame.

ing the bladder. In addition to this general treatment, nerve depressants are used in the treatment of poisoning by convulsants, and nerve stimulants are used in the treatment of nerve depressants. Irritants are diluted as quickly as possible and demulcents used to lessen the irritation. Cathartics are not given after poisoning by irritants if, as is usually the case, they induce purging.

THE NERVOUS SYSTEM

Such a large number of drugs obtain their effects by their actions on the nervous system that it will be well to antecede their study with a brief review of the structure and functioning of this system.

The nervous system is considered under **two main divisions,** known as the *cerebro-spinal* or *voluntary system* and the *autonomic* or *involuntary system.*

The **cerebro-spinal division** includes the portions of the brain and spinal cord and their nerves which are concerned with mental or psychic activities (including sensation) and the control of the skeletal muscles. The **autonomic system comprises** the portions of the brain, spinal cord ganglia and nerves that control the heart's action and that of plain muscle tissue and glandular organs. **Plain muscle tissue** is contained in: The true skin or derma; the walls of the trachea and bronchi; the alimentary canal from the esophagus to the anus of the rectum; the spleen; uterus; urinary and gall bladders and the canals and ducts leading from these organs and from glands.

The unit of nerve tissue is the nerve-cell or neurone A neurone consists of a mass of protoplasmic matter known as the cell-body (but commonly referred to as the cell) and processes, termed dendrites and axis-cylinders or axons.

Dendrites are branching, usually short, outgrowths from cell bodies. **Axons** are straight, elongated processes, usually of some length. Axons that extend beyond what is known as gray matter acquire a sheath, known as the neurilemma and are then called *nerve fibers.* Some nerve fibers have a white semi-liquid substance between the neurilemma and the axon and such are termed *medullated fibers.* Fibers of this variety constitute the white matter of the brain and cord and the fibers of spinal and cranial

nerves which supply the skeletal muscles and sense organs and stimulate ganglia but, it is thought, only non-medullated fibers enter plain muscle tissue and glands.

Depending upon their function **neurones are classed** as afferent, efferent and connecting or association neurones. **Afferent neurones** are those over which impulses pass from the periphery to the brain and spinal cord; **efferent,** those over which impulses pass outward. Connecting neurones are those placed between afferent and efferent neurones. The branches of the majority of association neurones are short but numerous. The special purpose of these neurones is to diffuse passing impulses so that a relatively small number of afferent impulses can be discharged over many efferent neurones; for example, a small crumb in the larynx will only stimulate a few afferent fibers but the stimulus will be diffused over thousands of efferent fibers.

Afferent neurones that form part of sense organs—eyes, ears, etc.—are often called sensory neurones and, likewise, efferent neurones are sometimes given special names that suggest their function, those which transfer the impulses to muscles that cause them to contract being called *motor neurones;* those which transmit impulses to glands that cause secretion, *secretory neurones;* those which transmit impulses that inhibit either muscular activity or secretion, *inhibitory fibers.*

The peripheral endings of nerve-fibers with different functions vary in their character. The nature of these variations need not be gone into here further than to state that some (efferent) are adapted for the discharge of impulses into muscles and glands, and others (afferent) known as *receptors,* for the reception of different kinds of stimuli, *e.g.,* light, sound vibrations, cold, heat, pressure. Since there are differences in the structure of the different kinds of endings, certain drugs may affect some and not others or may affect the different ones in dissimilar ways.

The nerve-fibers extending between the central part of the nervous system and the skin, muscles and internal

organs are grouped together in cord-like structures known as nerves.

Some nerves consist of afferent fibers only and some of efferent, but the majority have both afferent and efferent and are known as *mixed nerves.* **Fibers that unite to form a nerve may arise** from different masses of gray matter (usually termed *roots* or *nuclei* or *ganglia*) or from cells that are all grouped in one mass, and in either case the fibers constituting the nerve may branch from it and supply quite distant parts of the body that have dissimilar functions.

The structure of the nerve cell-bodies in different parts varies and, therefore, as in the case of the peripheral endings, drugs that affect one group may not act upon others or may do so with dissimilar effects. The protoplasm of the dendrites is similar to that of the cell bodies from which they arise, but that of the fibers and endings are different and, therefore, drugs may act upon the cells without affecting the fibers or their peripheral endings or, if they act upon both, the effects may vary. But the results of stimulation or of depression upon cells or peripheral endings will be the same.

As the gray matter contains the cell-bodies and their dendrites and axons and branches of the latter, known as *collaterals,* it is in the gray matter that nerve impulses pass from the axons of afferent fibers to the dendrites of connecting and efferent fibers. This functional union of the processes of different neurones is termed a *synapse.* The term *functional union* is used because it is thought the processes of different neurones do not come into actual contact with each other.

It is believed that it is **at the synapses that the passage of impulses is regulated.** This regulation involves several factors: (1) It prevents impulses passing back over the neurones by which they have been transmitted. (2) It determines the facility with which impulses pass. Normally, the synapses offer a slight amount of resistance to the passage of impulses, but under some conditions,

both physiologic and pathologic, and by the influence of drugs which depress the neurones, the resistance to the passage of impulses is increased and the individual does not respond readily to stimuli, while other conditions, and the influence of drugs such as caffeine and strychnine, lessen the resistance to the passage of impulses and the individual then exhibits the condition known as nervous and responds too readily and forcefully to stimuli; *e.g.*, jumps or exclaims at a slight noise. Such a condition may, probably, also be caused by primary stages of depression because this affects self-control. **The conditions responsible for affecting the passage of impulses** are unknown but the brains of animals which have been fatigued, and those which have not, show differences in the condition of the cell-bodies and dendrites and fatigue is one of the conditions that retards the passage of impulses. (3) It is thought that it is chiefly at the synapses that nerve-impulses make the impression on the brain and cord which compel the passage of later impulses, arising from similar stimuli, to take the same course, thus making it almost inevitable that an act which is repeated a few times in the same way will always be done in like manner on future occasions. In other words, it is probably at the synapses that nerve-impulses make the modifications which constitute the basis for habits and, to some extent, for characters.

Masses of gray matter containing the cell-bodies of the fibers which transmit impulses to organs and, thereby, control their functions are known as **nerve-centers.**

Fibers do not as a rule **extend directly from centers to organs,** but form synapses with neurones in other masses of gray matter which constitute, as it were, relay centers or stations. For example fibers from centers in the part of the brain known as the medulla oblongata form synapses with neurones in the cord and the fibers from those form synapses with neurones in the masses of gray matter in the abdominal and thoracic cavities known as *ganglia.* Also, some so-called centers are merely indispensable distrib-

uting stations. For example, if the mass of gray matter known as the center of vision is destroyed, sight will be lost, even though the eyes are perfectly normal, but, nevertheless, this center, it is thought, is merely the location where the fibers of the optic nerve form synapses with other fibers which, like those in the center of sight, or vision, have been acted upon in some unknown manner by previous impulses so that the associations (memories) of things seen have been formed.

The tissue of the **brain** is so distributed that definite, but connected, **divisions** are observed. The main ones are known as: The cerebrum, which is the upper portion; the cerebellum, below the dorsal portion of the cerebrum; the midbrain, under the central portion of the cerebrum; the pons, under the latter; the medulla below the pons and continuous with the spinal cord.

The outer surface of the cerebrum, known as the cortex, consists chiefly of gray matter. This includes centers that are necessary for (1) the reception and distribution of sensory impulses; (2) the coördination of muscular movements; (3) mental or psychic phenomena. The centers governing these three classes of functions are grouped in fairly definite masses and those which are specially concerned with sensation are termed *sense areas;* those concerned with movement, *motor areas;* those essential for consciousness, *association areas.*

The centers in the association areas are connected by nerve-fibers with each other and with sense and motor areas but not, except through the intervention of sense and motor areas, with the periphery. The sense areas thus act as doors for the entrance of impulses to the association areas and the motor areas as doors for their exit. It is probably in the association areas that the impressions are made in the protoplasm by things heard, seen and thought which constitute our intellectual memories. Also, these areas are thought to be the seat of the activities known as imagination, judgment, reasoning, self-control and other acts of consciousness.

By imagination is meant the synthesis of memories into original combinations or ideas or, in other words, mental pictures, formed from memories, but not exact reproductions of the data of the memories. Such mental activity does not necessarily require concentration of the attention. In its lowest form it consists simply in trains of images, suggested by one another or by outward stimuli, with little attempt at reconstruction. Examples of higher types are, the imaginings of plots, conversations and the like, and the mental visions of scenery that form in the author's brain; and the picturing of physical forces that the scientist indulges in, but, so long as the process is purely that of imagination there is no attempt at the selection of ideas, or of verification of their truth. The latter processes belong to the faculties known as **judgment** and **reasoning**, both of which require more or less conscious effort and concentration of the attention and are likely to check the freedom of the imaginative process. **Self control** implies conscious inhibition of response to stimuli. The powers of judgment, reasoning and self control develop later in life than the faculty of imagination and are more dependent upon exercise; also, they require more conscious effort. Such faculties are often referred to as the higher **intellectual capacities** and it is such capacities that are first reduced by physiologic (as tiredness), pathologic (disease) or drug depressants.

Nerve centers are only active when they are stimulated and, therefore, as stimuli enter the association areas through the sensory centers, the former will be rendered inactive, and unconsciousness thus induced, by drugs that depress the sensory centers, as well as by those that act upon the association centers directly. In fact, when unconsciousness is due to depression of the association areas only, unless the depression is very profound, the individual will be aroused by strong stimuli, such as pain.

Also, **depression of sensory centers** will render the perception of sensation—pain, sight, hearing, touch, etc.—less acute. It will have much the same effect as the reduction

of external stimuli; for example, a mild depression will have about the same result as when an individual reclines at rest in a warm, quiet, dark room. **Stimulation of sensory centers,** of course, heightens the appreciation of sensation.

The motor areas of the cerebrum, it is thought, contain centers that are of importance to the incitement of voluntary movement and to muscular coördination, *i.e.*, the control of the muscles which makes the right ones for the performance of an act work in unison.

The cerebellum also helps to control muscular coördination and its activity is essential for muscle tone. Depression of the cerebellum and the motor areas of the cerebrum will thus result in imperfect muscular coördination; an example of the result of this is the staggering gait of a drunken man.

The midbrain consists chiefly of fibers passing to and from different parts of the brain and between the brain and cord, and of small separated masses of gray matter that serve as relay stations for many of these fibers; *i.e.*, many of the fibers terminate in this gray matter but form synapses with other neurones which transmit their impulses onward. There is also in the midbrain a mass of gray matter that is influenced by the temperature of the blood passing through it and, in response to such influence, sends impulses to the centers which influence heat production and heat loss. This is known as the heat *regulating center*. There are also other centers in what are known as the *thalami* (small masses of gray matter in the under surface of the cerebrum, just above the midbrain) that are affected and react in the same manner. The action of these heat regulating centers has been already discussed in the paragraph on Antipyretics.

The pons, like the midbrain, consists chiefly of nerve-fibers and scattered masses of gray matter some of which contain the cell-bodies of cranial nerves.

The **medulla** consists of bundles of nerve-fibers, passing to and from the brain, and of masses of gray matter

(some of which are the nuclei of cranial nerves) which control the vital body functions, such as the rate of the heart action, respiration, the caliber of the blood-vessels, the activity of many of the secretory glands, swallowing, and sucking, also coughing and vomiting.

There are twelve pair of cranial nerves. They pass through foramina in the skull and innervate the sense organs, skin, muscles and glands of the head and neck, and the tenth nerve, known as the *pneumogastric* and as the *vagus*, innervates the viscera designated in the section describing the autonomic system.

The spinal cord is contained in the spinal canal, *i.e.*, the canal of which the bodies of the vertebræ form the front wall and the vertebral arches the back wall. The interior of the cord consists of gray matter, massed around a minute central canal, and its exterior chiefly of columns of nerve-fibers.

The fibers in the columns **on the ventral or anterior** (front) **surface** have their origin in the brain and terminate in the ventral gray matter. This gray matter contains the cell-bodies (with their dendrites) from which the fibers arise that pass through the openings between the vertebral arches and constitute the efferent fibers of the spinal nerves.

The columns **on the dorsal or posterior surface of the cord** contain the afferent fibers that have their origin in the gray matter of the dorsal portion and form synapses in gray matter in different parts of the brain. The dorsal gray matter contains the cell-bodies (with their dendrites) from which these fibers arise and also axons of the afferent spinal nerves. The cell-bodies of the latter constitute the spinal ganglia, small masses of gray matter in the vertebral foramen (spaces between the arches). The fibers extending from these ganglia (they are not to be confused with the sympathetic ganglia) to the periphery constitute the afferent fibers of the spinal nerves. Thus an afferent fiber of a spinal nerve has no dendrites, but two axons, one of which, as a nerve-fiber, extends to the

periphery and the other enters the gray matter of the cord.

The sides of the cord consist chiefly of connecting neurones over which impulses coming into the cord over the afferent fibers of spinal nerves are transmitted to the efferent fibers and to cells in different levels of the cord.

If, as the result of a drug, injury or disease, cells in the gray matter of the posterior surface of the cord or their fibers are depressed, sensation in the parts of the body below the affected area will be lost, but unless anterior neurones are also affected there will be no paralysis.

The chief functions of the spinal cord are: (1) The transmission of impulses between the brain and the spinal nerves and the rami (branches which connect the voluntary and involuntary systems). (2) Reflex action. (3) It contains centers which help in the control of the viscera.

By reflex action is meant an involuntary act or physiological response produced by nerve impulses that have travelled over afferent fibers to nerve-centers and been discharged thence over efferent fibers to the affected muscles or glands. Though a reflex is involuntary, it will be associated with consciousness if the impulses are also transmitted to the association areas of the cerebrum.

There is a constant inflow of nerve impulses from the exterior of the body—the skin, eyes, ears, muscles—that induce no observable response, but which result in the discharge of light impulses into the muscles and thus help to maintain the condition of light contraction or readiness to contract that is known as **muscle tone.** When the tissue of the cord is in a depressed condition, impulses do not pass as readily as usual.

Stimulation of the cord usually means that some unknown conditions are caused which facilitate the passage of impulses through and from the cord. Over stimulation will result in such free passage of impulses that very slight stimuli will induce muscular twitching and, if very pronounced, convulsions.

The regions of the cord and the spinal nerves are named

to correspond with the vertebræ through which the latter pass. Thus there are the cervical, thoracic, lumbar and sacral regions.

The autonomic portion of the nervous system, as previously stated, controls the action of plain muscle tissue and of the glands that are under nervous control. Knowledge of the relationship of the actions of the nervous system and the glands of internal secretion other than the suprarenal capsules, is still indefinite. The parts of the body containing plain muscle tissue were mentioned on page 70.

Before reviewing the functions of this system it will be well to recall **the distribution of the ganglia and nerves** comprising it.

There are, it will be remembered, three sets of ganglia in the thoracic and abdominal cavities. (1) The vertebral ganglia, known also as the sympathetic ganglia and the ganglionic chain, (2) the prevertebral ganglia, (3) the terminal ganglia.

The vertebral ganglia consist of masses of gray matter, connected to each other with nerve fibers, that extend, like a chain, on either side of the spinal column, in the thoracic and abdominal cavities. White nerve-fibers, some of which have their origin in cells of the gray matter of the cord and others in the ganglia serve to connect the ganglia in the thoracic and upper lumbar regions with the cord. These fibers, known as the *white rami* (branches) serve as a passage way for impulses, afferent and efferent, passing between the cord and ganglia. Non-medullated fibers that have their origin in these ganglia (the gray rami) pass out and join the spinal nerves or those from the cervical ganglia, upward to join certain cranial nerves. These are the route for the passage of impulses from the ganglia to the plain muscle tissue and glands outside of the trunk cavities. Other non-medullated fibers that have their origin in these ganglia pass into the cavities and help form the splanchnic (visceral) nerves. Some fibers pass directly into the organs and others form synapses with

neurones in the prevertebral and terminal ganglia. **The prevertebral ganglia** are scattered through the thoracic and abdominal cavities and are the origin of a large number of fibers that extend between the different ganglia and organs. They are so numerous and widely distributed that they appear as networks (plexuses). Those arising in any one ganglia may supply several organs and thus they coördinate the activity of organs so that those engaged with the same function are influenced by the same stimuli. Some of the cells of these ganglia receive their efferent stimuli from the vertebral ganglia and others from the vagus nerve, or some of those supplying the pelvic organs, from the pelvic nerve. **The terminal ganglia** are situated in the walls of the organs they supply and fibers pass from them into the organs. They are stimulated by impulses passing through either of the other ganglia or over the vagus or pelvic nerves.

The parts of the nervous mechanism constituting the autonomic system are classified in two subdivisions named the *sympathetic* and the *para-sympathetic systems;* the latter is known also as the *enteral system* and as the *great vagus*—after the vagus nerve which constitutes a large portion of this division.

The parts classified as the sympathetic system are those which are stimulated by the drug adrenaline and by strong unpleasant emotions, such as rage and fear, and by severe pain.

The physiological reactions to such emotions as rage and fear are: The bronchial tubes are relaxed (this favors rapid breathing); the heart beats more strongly; the blood-vessels of the abdominal viscera are contracted and more blood is thus forced to the brain, heart, lungs and muscles; the secretion of perspiration and adrenaline is increased; the liver yields more glucose to the blood (these reactions are nature's provision for the natural animal response to such stimuli as rage and fear; *viz.*, fight or flight; for they tend to provide the muscles with energy material and to facilitate the removal of the excess

waste and heat that increased muscular activity involves). Also, the radial muscles of the irises are contracted and this dilates the pupils; and alternate contraction and relaxation of the uterine muscle may be induced. At the same time, the contraction of the muscle tissue of the stomach and intestines, of the bladder, external genital organs and, as previously implied, of the larynx and bronchial tubes is reduced; and the secretions necessary for digestion, other than sometimes saliva, are inhibited.

The parts of the nervous system involved in these reactions are: The cardiac accelerator and vasoconstrictor centers in the medulla, neurones in the thoracic and lumbar sections of the cord, the sympathetic ganglia and their nerves and some of the other ganglia.

The remainder of the nerve supply to the viscera constitutes the **para-sympathetic system.** There are two main divisions of this system, termed the *cranial* and the *sacral divisions.* The former consists of the vagus nerve and some neurones associated with the third, seventh and ninth cranial nerves. The sacral division consists of neurones that have their origin in the sacral portion of the cord, the fibers of which constitute what is known as the pelvic nerve. **The vagus nerve supplies:** Both efferent and afferent inhibitory fibers to the heart (the afferent fibers arise from cell bodies contained in minute ganglia situated in the heart muscle; these are stimulated when blood pressure becomes extreme and the consequent impulses are transmitted to both the vagus and vasoconstrictor centers and, therefore, tend to slow the heart action and lessen the contraction of the blood vessels); afferent and motor fibers to the pharynx, esophagus, stomach, small intestine, larynx, bronchi and lungs; motor fibers to the muscle tissue in the spleen and liver; secretory and vasodilator fibers to the mucous membrane and glands of the stomach and small intestine. **The third cranial nerve supplies** the ciliary muscles of the eyes and the circular muscles of the irises with motor fibers. **The seventh and ninth cranial nerves** supply the mucous membranes of the nose and

mouth and the salivary glands with secretory and vaso-dilator fibers. **The pelvic nerve** supplies motor fibers to the large intestine and bladder. It is thought probable that all the fibers of these nerves which supply the viscera form synapses in the prevertebral or terminal ganglia and do not themselves enter the organs.

Stimulation of the sympathetic	Stimulation of the para-sympathetic
Strengthens and increases the rate of the heart action.	Slows and weakens the heart action. (See page 55.)
Contracts the blood-vessels except those of the brain, heart and lungs.	Probably dilates blood-vessels in the alimentary canal and possibly some others. (See page 56.)
Increases the change of glycogen to glucose.	Inhibits the change of glycogen to glucose.
Lessens the secretion of the gastric and intestinal juices and possibly the pancreatic juice and bile and usually the saliva.[1]	Increases the secretion of saliva, the gastric and intestinal juices and, slightly, the pancreatic juice.
Lessens the motor activity of the stomach and intestines but contracts the sphincter muscles.	Increases the motor activity of the stomach and intestines and relaxes the sphincters.
Lessens the contraction of the bladder.	Promotes contraction of the bladder.
Relaxes the muscle tissue of the trachea and bronchial tubes.	Contracts the trachea and bronchial tubes.
Dilates the pupils and relaxes the ciliary muscles of the eyes.	Contracts the pupils and the ciliary muscles.

In all cases **stimulation of inhibitory fibers** supplying an organ lessens the activity of the latter and depression of

[1]Some drugs that stimulate the sympathetic do not check the mouth secretions but its stimulation by unpleasant feelings, as worry and vexation, and strong emotions, as fear and anger, are likely to do so. A practical application of this was made in olden times in India, in what was known as "the ordeal of rice." The suspected persons were given rice to chew and after a time were required to spit it out. If any one ejected it dry, he was judged guilty it being considered that fear of discovery had stopped the flow of the liquid which keeps the mouth moist.

the inhibitory mechanism has the same effect as stimulation of the motor or secretory mechanism, namely, increased activity. Very little is as yet positively known regarding the manner in which inhibition is promoted.

By comparing the results of stimulation of the sympathetic and para-sympathetic divisions of the autonomic system it will be seen that the action of each one in most cases, antagonizes that of the other. Important examples are seen in the foregoing table:

Parts of the body that, as far as known, are supplied only with fibers belonging to the sympathetic system: The sweat gland, the pilo-motor muscles, the uterus and the suprarenal capsules, but the sweat glands and the uterus are affected by some drugs that act upon the parasympathetic system.

The only nerves supplying the kidneys are those innervating the blood-vessels.

In order to understand the action of drugs upon the viscera it is necessary to appreciate the following facts: (1) The ganglia through which impulses pass to the viscera are never stimulated directly by afferent impulses, *i.e.*, all impulses reaching them are transmitted through centers in the cord and brain and, therefore, any drug that acts as a general stimulant or depressant to these organs may affect the viscera to some extent. (2) The centers of the autonomic system receive stimuli from fibers belonging to the sense organs and, thus, the cerebrospinal system. (3) Pronounced stimulation of one division of the autonomic system is likely to influence some part of the other; for example, (1) pronounced contraction of the blood-vessels stimulates the vagus, as described on page 55; (2) strong stimulation of the vagus fibers supplying the trachea and bronchi gives rise to the spasmodic contractions seen in asthma, and the distress and pain thus occasioned stimulates the sympathetic system. (4) Depression of one division of the autonomic system will have the same results as stimulation of the other on organs in which the systems oppose each other.

(5) Especially in the case of the para-sympathetic division, all parts are not necessarily affected by a stimulant or depressant, *e.g.*, the vagus supply to the heart can be stimulated without affecting the supply to the alimentary tract, and the vasoconstrictor supply to the skin can be stimulated without affecting that of the viscera and vice versa.

DRUGS WHICH OBTAIN THEIR CHIEF EFFECTS BY STIMULATING NERVE CENTERS

The drugs which obtain the majority of their important effects by stimulating nerve-centers are caffeine and strychnine. There are a number of other medicines which produce some important effects in like manner, but, as they are more commonly used for the results of their other actions, they are generally otherwise classified.

CAFFEINE

Caffeine or *trimethylxanthin* is a mildly basic alkaloid that, in its chemical structure, is similar to waste substances found in the urine and in animal tissues. It is prepared chiefly from damaged tea leaves, but it is also contained in a number of other plants, especially the berry of the coffee tree and in the cola (or kola) nut.

Preparations and dosage:

Caffeine, 1–5 grs. (0.06–0.3 gm.).

Caffeine citrate, 2–8 grs. (0.13–0.5 gm.).

Effervescent caffeine citrate, 1℥ (4.0 gm.).

Caffeine sodium benzoate (2–5 grs. (0.12–0.3 gm.) unofficial).

Guarana, fluidextract of, 30 m.–2 (2.0–8.0 c.c.). *This contains caffeine and tannin.*

Fate in the Body.—Caffeine is fairly readily absorbed from the stomach and intestines, its effects being evident in about from ½ to 1 hour. It is changed to urea in the body and in this form eliminated rapidly by the kidneys.

Actions:

Caffeine Stimulates: The cerebrum, including (*a*) the association areas, *i.e.*, those which control intellectual functions, as judgment, reasoning, imagination, will power, etc.; (*b*) sensory areas; (*c*) motor areas. The res-

piratory center, and, slightly, the vasoconstrictor and vagus centers and the spinal cord. Also, it stimulates the skeletal muscles and in large doses it may stimulate the heart muscle to a slight degree. It increases the activity of the kidneys by, it is thought, stimulating the tubule cells and dilating the renal blood-vessels.

Results of actions:

As the result of its action on the cerebrum, caffeine will overcome mental fatigue, it will promote wakefulness and render the mind more alert so that memory is aided, the imagination quickened, ideas and the words in which to express them are more readily conceived. Moderate doses of caffeine will increase the power of self-control and facilitate judgment and concentration of the attention, but large doses interfere with these faculties, because the mind becomes so active that concentration, which is necessary for judgment and reasoning, is interfered with. If caffeine is taken when the brain is in its normal condition and not fatigued, even moderate doses may have the effect of large doses. The stimulation of the sensory areas of the cerebrum renders the perception of sensory stimuli, such as sight, hearing, smell and pain, more acute. It can be easily appreciated that many of the effects of cerebral stimulation may be undesirable in illness.

The stimulation of the respiratory center causes an increase in the rate and depth of breathing. This is one of the most valuable therapeutic effects of caffeine.

The **stimulation of the vasoconstrictor center,** though slight, tends to favor contraction of most of the vessels that are under the control of the vasoconstrictor center (those of the brain, lungs and heart are not) and thus to cause a slight, transitory rise of blood pressure. The **renal blood-vessels** are relaxed; the reason for this is not known, but it is thought to be the result of the increased activity of the kidney cells. There will be an increased amount of blood in the organs in which the vessels are not contracted.

The stimulation of the **vagus** tends to slow the heart

action, but, sometimes, especially in susceptible individuals, the general nerve stimulation will overcome the vagus effect, which is not very strong, and the rate of the heart may be accelerated and, occasionally, palpitation is induced.

As a rule the **heart action,** and thus the pulse, becomes slightly stronger. This may sometimes, possibly, be due to a direct stimulation of the heart muscle, but it is thought to be more commonly the result of the increased blood supply (and thus nourishment and oxygen) that the heart receives and the increased blood pressure.

The stimulation of the **spinal cord** facilitates the passage of impulses to and from the brain and between the cord and muscles and the viscera. The increased flow of impulses to the muscles improves their tone and, after overdoses of caffeine, may cause muscular twitching. Caffeine, however, does not stimulate the spinal cord to as great an extent as strychnine.

The direct action of caffeine on the **skeletal muscles** also serves to promote their tone and it favors an increase in the speed and accuracy of muscular movements and tends to retard the onset of fatigue. If an excessive amount of caffeine is taken, however, eventually muscle fatigue may be increased.

As the result of its action on the **kidneys,** caffeine causes diuresis.

To summarize:

The more important good effects of caffeine may be classified under two headings, (1) those for which it is used by practically normal individuals and (2) those for which it is used in illness. They are: (1) **For a relatively normal person:** Lessening of fatigue; stimulation of the intellectual faculties, when these are depressed; relief of headache, especially that due to mental strain. Such relief is thought to be the result of the improved circulation in the brain and of the relief of the mental strain afforded by the increased ease of thought and power to concentrate the attention which follows the cerebral stimulation. (2) **In illness:** Stimulation of breathing;

increased blood-pressure with consequent improvement in the circulation and strengthened pulse beat, the rate of the pulse may undergo little change, but it may be either slightly increased or slowed; increased excretion of urine.

Bad effects that may follow the use of caffeine are: Wakefulness, restlessness, palpitation and other nervous symptoms; hyperacidity of the gastric juice; nausea; if a patient has pain, its perception will be intensified; the cerebral stimulation may render a sick person more conscious of the precariousness of his condition.

The more common therapeutic uses of caffeine are: To stimulate the respiratory center when it is depressed or when breathing is difficult from any cause. To improve the circulation in shock and collapse. To induce diuresis. To stimulate the cerebrum in some cases of mental depression. To prevent or overcome excessive fatigue. As an antidote for poisoning by drugs which depress the nerve-centers. Even the effects of caffeine that, under ordinary conditions, are unfavorable are of service for this purpose.

Overdosing and Poisoning.—Acute poisoning by caffeine is very rare because the drug is not strongly toxic and it is rapidly excreted. If it is taken in large amounts, however, or even in more than slightly moderate doses for an extended period (either as the drug or in coffee) some or all of the following symptoms may follow:

Restlessness; insomnia; inability to concentrate the attention; headache; frequent pulse; palpitation; profuse diuresis; too free response to reflexes which is shown by twitching of the muscles and, for example, the individual jumps or exclaims on hearing a noise and gives evidence of irritation on the slightest provocation. Both of these examples show a lack of inhibition which, it will be remembered, caffeine, in moderate doses, tends to stimulate.

If poisonous doses are taken, the above symptoms may be followed by delirium, convulsion and, finally collapse, due to the depression of nerve centers which almost invariably follows their excessive stimulation.

COFFEE AND TEA

Roasted coffee contains about 0.6 to 2.0 per cent. caffeine, a small amount of caffeole, a volatile oil to which its flavor and odor are due, and a varying, but relatively large, amount of caffeotannic acid and extractives.

Tea contains 1–4 per cent. caffeine, a small amount of theophyllin, a volatile oil to which its flavor and odor are due, tannic acid. Green teas have less caffeine and more tannin than black teas.

Though tea leaves contain more caffeine than coffee, there is, as the beverages from these substances are ordinarily prepared, less caffeine in a cup of tea than in a cup of coffee; a cup of tea containing about 1–2 grains (0.06–0.12 gm.) and coffee 1½–3 grains (0.1–0.2 gm.) of caffeine.

The volatile oil of coffee is slightly stimulating to the cerebrum and thus a slight stimulant effect may be expected even from preparations such as Kaffee Hag from which the caffeine has been extracted. Also, the volatile oil and extractives have a slight irritant action in the alimentary canal and thus tend to exert a slight laxative effect and, in susceptible people, they may promote hyperacidity of the gastric juice and, when a person is indisposed, increase nausea. The caffeotannic acid does not precipitate albumins and alkaloids, as does the tannic acid in tea, and thus coffee cannot be used as a substitute for tannin in poisoning by alkaloids. It does, however, tend to retard absorption and digestion, but, unless the coffee is boiled, there will be very little of this present in the beverage.

The volatile oil of tea is less irritating to the alimentary tract than that of coffee and tea can often be taken when coffee causes nausea. In fact, a cup of hot tea, without cream or sugar, will often overcome nausea, especially if the patient likes tea. Tea has no laxative effect.

The tannic acid of tea is astringent and it precipitates protein, thus it tends to retard digestion and absorption,

but if the beverage is properly prepared it will not contain enough tannin to do this to a harmful degree. The tannic acid also precipitates alkaloids and thus strong, boiled tea (preferably green) is used in poisoning by alkaloids when the pure tannin cannot be obtained.

NUX VOMICA AND STRYCHNINE

Nux vomica is obtained from the seeds of several species of the trees classed as the *Strychnos* which grow in the East Indies and some other tropical Oriental countries. The seeds are known as poison nut and, because they are of a gray color and button-shape, Quaker buttons.

The active principles of nux vomica are the alkaloids strychnine and brucine. These both have the same actions, but brucine is only about ⅓ as strong as strychnine.

As the therapeutic actions of nux vomica are, of course, due to its active principles, they are practically the same as those of strychnine, but weaker.

Preparations and dosage:

Extract of nux vomica, ⅙–1 gr. (0.01–0.06 gm.).

Fluidextract of nux vomica, 1–5 m. (0.06–0.3 c.c.).

Tincture of nux vomica, 5–15 m. (0.3–1.0 c.c.).

Strychnine, 1/40–1/15 gr. (0.0016–0.004 gm.).

Strychnine sulphate, 1/40–1/15 gr. (0.0016–0.004 gm.).

Strychnine nitrate, 1/40–1/15 gr. (0.0016–0.004 gm.).

Non-official preparations:

Iron and strychnine citrate 2 grains (0.13 gm.).

Elixir of iron, quinine and strychnine phosphate, 1–2 drams (4.0–8.0 gm.).

Syrup of iron, quinine and strychnine phosphate, 1–2 drams (4.0–8.0 gm.).

Compound laxative pills (containing aloin, belladonna and strychnine), 1–2 pills.

Administration.—When used as tonics, strychnine and nux vomica are given by mouth and before meals and nothing must be done to disguise their taste. When used for other purposes the time of administration is not of importance.

Fate in the Body.—Strychnine is readily absorbed. Part of a dose is oxidized in the tissues and the remainder is eliminated in the urine. Its excretion is moderately rapid, traces being detected in the urine soon after a dose is given, but, if large doses are taken for any length of time, enough may be retained in the body to cause cumulative poisoning.

Actions:

In the mouth, strychnine stimulates those taste-buds which are influenced by bitter substances.

After absorption, it stimulates the spinal cord and, slightly the cerebrum, especially the sense areas; sometimes it tends to stimulate the vagus, vasoconstrictor, and respiratory centers and apparently the vasodilator centers supplying the vessels in the skin. Some investigators believe that, in therapeutic doses, strychnine merely increases the sensitiveness of the vasoconstrictor and respiratory centers, thus rendering them more easily stimulated by other drugs and by the physiological stimuli which normally affect these centers. Toxic doses first stimulate and then depress the respiratory center. Strychnine stimulates the cord more, and the brain less, than caffeine.

Effects of actions of therapeutic doses:

By its action on the taste-buds, strychnine promotes the secretion of saliva and gastric juice and stimulates the appetite and thus aids digestion. This is further discussed under bitters.

The stimulation of the spinal cord permits impulses to pass more readily through this organ and out along motor nerves. The increased amount of stimulus thus thrown into the **muscles** increases their tone. Plain muscle tissue, especially that of the stomach, intestines and bronchi, is similarly affected; thus the motor activity of the stomach and intestines is increased and digestion, absorption and defecation favored. The effect on the bronchial muscle is of value when this is relaxed, but, it is undesirable in conditions such as asthma.

The increased muscular contraction augments **metabolism.** Ordinarily, this would cause a rise of **temperature,** but, as the superficial blood-vessels tend to become somewhat relaxed, the amount of blood near the surface of the body is increased and the extra loss of heat which this involves is proportionate to the increased heat production, provided this is not excessive, as is the case following toxic doses of the drug.

The **pulse** tends to become somewhat slower, due to the stimulation of the vagus, and, after several doses of strychnine have been taken, the circulation may be improved. This is thought to be due chiefly to the increased muscle tone.

Ordinarily, therapeutic doses have not much effect upon **breathing,** but the rate and depth may be slightly increased, especially if they have been below normal, and strychnine is thought to aid the action of other drugs in overcoming depression of the respiratory center due to narcotic drugs.

The results of **cerebral stimulation** are similar to those induced by caffeine, but much less marked.

To Summarize the Good Effects that may be Obtained from the Use of Strychnine.—There may be improvement in the appetite and digestion; in the action of the bowels; in general muscle tone and the circulation of the blood and lymph with a consequent improvement in body nutrition. In order to derive such benefit from strychnine, however, it is necessary for the individual to have an adequate supply of nutritious food and to be in a state to respond to the increased metabolism which the heightened muscular tone involves. The use of strychnine without these requirements has been likened to "whipping a horse to make it get up after it has fallen from exhaustion."

The more common therapeutic uses of strychnine are:

As a general tonic.

To increase the appetite and aid digestion; nux vomica is generally used for this purpose.

To increase muscle tone in some forms of paralysis and the tone of the intestine in chronic constipation.

As a physiological antidote in the treatment of poisons which depress the spinal cord and respiratory center.

Toxicology:

The chief symptoms of overdosing by strychnine are due to the lowered resistance[1] to the passage of impulses in the cord and the excessive discharge of impulses into the muscles. They are: Restlessness; nervousness, which is shown especially by intense reflex response to stimuli;[2] stiffness and twitching of muscles, particularly those of the face; and, especially when overdosing is due to cumulative effects, diarrhea.

Following toxic doses there will be: Stiffness of the muscles of the face and neck and spasmodic twitching of these and other muscles followed by a convulsion in which all the voluntary muscles are involved, but, as the extensor muscles are stronger than their opponents, their action is most evident and the legs and arms become rigid and extended and the back and head drawn backward so that the body becomes arched. The eyes are open and the muscles of the face drawn up in such a manner that a ghastly grin is caused. At first the convulsion is tonic (*i.e.*, the muscles remain constantly rigid), but after a time it becomes clonic (*i.e.*, the muscles periodically relax and contract) and this condition is followed by extreme relaxation of the muscles and the patient lies exhausted, but the slightest stimulus, such as a light, a jar of the bed, even movement of the covers or a draft of air, may cause another convulsion, for the convulsions are the result of the abnormal ease with which impulses pass through and from the cord. The face becomes cyanotic because the spasms of the chest muscles interfere with breathing. Due to the increased metabolism, as the result of the excessive muscular contraction, the temperature may become exceedingly high. As the cerebrum is

[1] This was explained on page 73.

[2] This was explained on page 78.

stimulated, the patient is likely to be conscious and his perception of pain so increased that he may suffer agony during the convulsions.

Unless treatment is effectual, convulsions become more and more frequent and the patient dies either from exhaustion or from asphyxia and the latter may be due either to interference with breathing during a convulsion, or to exhaustion of the respiratory center.

Treatment for Poisoning.—If the drug has been taken by mouth, the stomach is lavaged and strong tea or preferably tannic acid is given and in a few minutes removed by lavage. This is essential because the tannate of strychnine that is formed is not altogether harmless and it will be absorbed, though not as readily as the medicinal strychnine salts. If tea is used the lavage must be particularly thorough because the caffeine in the latter, if absorbed, will stimulate the already over-stimulated nerve-centers.

The patient is catheterized at relatively short intervals to prevent the reabsorption of any strychnine from the bladder.

The doctor is likely to give an intravenous infusion, to hasten the elimination of the drug, and an intraspinal injection of magnesium sulphate, this drug having the opposite of effect of strychnine on the spinal cord.

Drugs that act as nerve sedatives, especially bromides and paraldehyde, are prescribed. Morphine cannot be used because of its depressing action on the respiratory center.

Absolute quiet is one of the most essential items in the treatment and the room must be dimly lighted and free from draughts, though well aired.

If treatment is not started before the symptoms of poisoning are evident, which will be in from 10 to 20 minutes from the time the dose is taken, the patient is generally anesthetized before giving lavage, etc., for, otherwise, the treatments may induce a convulsion.

CARBON DIOXID (CO_2)

Though carbon dioxid is very rarely used to stimulate nerve-centers, and very frequently employed for the effects of its local actions and, therefore, according to the classification followed in this book, should be grouped with drugs that are used chiefly for the effects of their irritant action on mucous membranes, it is described here because knowledge of the symptoms that follow the administration of an excessive amount by inhalation, or without an adequate quantity of oxygen, will be of help in understanding the symptoms of poisoning by a large number of drugs discussed later; for, as stated in the section on Toxicology, poisonous doses of almost all drugs interfere to some extent with, either or both, the elimination of carbon dioxid from the system and the intake of oxygen. Another fact that makes its description here appropriate is that, though it is used to stimulate nerve-centers, its actions are very similar to those of the general anesthetics described in the section following, an important difference being that carbon dioxid can be so administered that a moderate degree of stimulation can be maintained for some time and depression need not be induced. Like the anesthetics, carbon dioxid can only be given by inhalation by those who are specially instructed.

Carbon dioxid is a heavy, tasteless, odorless, colorless gas. At a low temperature it can be readily condensed to a liquid and even solidified. It is freely soluble in water and it combines with water to form an unstable compound with a slightly acid reaction, that is known as *carbonic acid.*

Carbon dioxid is formed whenever organic matter is burned or otherwise decomposed in the presence of air or of free oxygen and also when the inorganic salts known as carbonates are heated or interact with acids.

Actions.—In more than moderate concentrations, carbon dioxid is irritant to the skin and mucous membranes. Its actions after absorption are only produced

when it is given by inhalation, in such case moderate amounts stimulate nerve-centers, especially the respiratory center, and the heart muscle, larger amounts are depressant.

Effects of Actions.—Liquid and solid carbon dioxid act as escharotics.

If a person remains for some time in a bath of water that is charged with carbon dioxid the skin may be sufficiently irritated to cause a slight dilation of the superficial blood-vessels and a consequent increase in the amount of blood in the skin, which is shown by a slight flushing of the latter.

Mucous membranes are more easily affected than the skin and thus beverages containing carbon dioxid increase the amount of blood in the membrane of the mouth and stomach, stimulate the secretion of mucus, saliva and gastric juice and cause the expulsion of gas from the stomach, in other words, they act as carminatives, as described on page 53. The extra blood in the membrane creates a sensation of warmth and well-being; digestion and absorption are aided, nausea may be overcome and patients with gastric disturbances who vomit other foods are often able to retain carbonated beverages, such as champagne, milk to which a carbonated water has been added or milks in which carbon dioxid has been developed by fermentation as koumiss and matzoon.

The carbon dioxid in beverages is readily absorbed from the stomach and intestines but it is so quickly eliminated through the lungs that the small amounts taken in this way have practically no **effect after absorption,** but **when carbon dioxid is given by inhalation, diluted with oxygen or air to 6 per cent.,** there may be some intellectual stimulation, the breathing movements become deeper and easier, there is a rise of blood pressure and slowing of the heart action. If the inhalations are too long continued, but an adequate supply of oxygen is given, the breathing becomes relatively slow and shallow; the pulse becomes weak, but remains slow; consciousness is lost; the muscles

relax. The conditions of this stage are very similar to those existing in ether and chloroform anesthesia. If they are allowed to progress collapse and death will ensue. If the oxygen supply is limited when carbon dioxid is given in excess, and in poisoning by drugs that in any way interfere with the absorption of sufficient oxygen, the stage of stimulation is transient and, in addition to the symptoms of depression just described, dyspnea and cyanosis become extreme, convulsions then follow and, unless the condition is ameliorated, collapse and death.

Therapeutic Uses.—Liquid and solid carbon dioxid are used to remove warts and similar growths.

Baths of carbonated water are used for the relief of chronic congestions.

Carbonated beverages and drugs, such as sodium bicarbonate, that release carbon dioxid when they come in contact with the acid of the gastric juice are used to relieve nausea. Carbonated food beverages are often used when other food is vomited and effervescent preparations are made of many drugs that are likely to cause nausea; as previously stated the effervescence is due to carbon dioxid that in the majority of such preparations, is formed by the interactions of an acid and an alkali.

Carbon dioxid is occasionally given by inhalation to stimulate the respiratory center, especially in the treatment of poisoning by drugs, such as opium, that depress it.

DRUGS WHICH PRODUCE THEIR CHIEF EFFECTS BY DEPRESSING NERVE CENTERS

NARCOTICS

Drugs which will depress the cerebrum sufficiently to produce unconsciousness without causing death, are classed as *narcotics.*[1]

The narcotics are usually considered in four sub-groups, viz.; (1) general anesthetics, those used to produce a sufficiently profound narcosis to allow surgical operations to be performed without causing pain; (2) alcohol; (3) hypnotics or soporifics, those which, in therapeutic doses, produce a state of stupor resembling sleep; (4) analgesics, those which relieve pain by depressing sensory centers the more powerful analgesics will also act as hypnotics.

GENERAL ANESTHETICS

The general anesthetics in common use are: Ether, chloroform, ethyl chlorid, ethyl bromide, nitrous oxid, pental, magnesium sulphate. Also various mixtures of these anesthetics are used, the most common ones being (1) what is known as A.C.E., which is a mixture of alcohol, chloroform and ether; (2) Anesthol, a mixture of chloroform, ether and ethyl chlorid.

HISTORY OF ANESTHETICS

Alcohol, in intoxicating quantities was, as far as is known, the first drug used to lessen pain during surgical operations. The use of nitrous oxid for the purpose was suggested by Dr. Davy in 1798, but his suggestion was not followed and a Dr. Wells, who advocated its use in 1844, is generally given credit for the discovery of the anesthetic properties of this gas. Ether was used by Dr. Long in

[1] From the Greek *narkē* = numbness.

1842, but he did not publish an account of his work and thus Drs. Morton and Jackson, who demonstrated the use of ether in 1845, are generally credited with its discovery. Chloroform was introduced by Dr. Simpson in 1847.[1]

ETHER

Ether is produced by the action of sulphuric acid on alcohol. It evaporates rapidly and the vapor, when mixed with air, is exceedingly inflammable. Therefore, ether must be kept in a cool place and it must never be brought near a flame.

Preparations and dosage:

For the therapeutic uses of ether other than anesthesia:

Ether, 10–15 m. (0.6–1.0 c.c.).

Spirits of ether, ½–1ʒ (2.0–4.0 c.c.).

Compound spirits of ether (Hoffmann's anodyne), 1ʒ (4.0 c.c.).

(*This contains ether, alcohol and ethereal oil.*)

Spirits of nitrous ether (Sweet spirit of niter) 30 m. (2.0 c.c.).

The amount of ether used for anesthesia depends upon the nature of the operation. As ether is eliminated very rapidly its use can be continued for some hours without bad effects if it is sufficiently diluted and only enough used to keep the patient in the condition known as the *third stage of anesthesia.*

Methods of Administration.—Small doses of ether and its compounds are given by mouth to obtain the effects of their action on the mucous membrane of the alimentary tract. Small doses of ether are also, occasionally, given by hypodermic to stimulate the heart action. To induce anesthesia, ether is usually given by inhalation, but it is also given by rectum, intravenously, and by intratracheal and intrapharyngeal insufflation.

As ether irritates body tissues, it must be diluted before

[1] This data was obtained from Pharmacology and Therapeutics or the action of Drugs. Cushny, Lea and Febiger.

or during administration. Water is the diluent used for administration by mouth; oil, for rectal administration; normal saline or Ringer's solution, for intravenous; and air, for inhalation and insufflation.

Fate in the Body.—Ether is rapidly absorbed by the blood from the mucous membranes of the alimentary tract, the lungs and subcutaneous tissues. It is distributed by the blood throughout the body, but is taken up chiefly by the cells of the cerebrum. The reason for this is thought to be a special affinity for certain lipoid substances that are far more abundant in the cerebral protoplasm than that of other tissues. Ether is rapidly excreted, chiefly through the lungs, but, also through the kidneys. A small dose will have left the body in about ½ hour and the amount used for anesthesia, during even an extensive operation, within 24 hours.

Actions:

Ether stimulates olfactory nerve-endings and certain taste buds.

Ether is very volatile and, when a part to which it is applied is exposed, the ether passes away so quickly that it does not affect the tissue otherwise than by abstracting the heat that it requires to further its evaporation. But ether dissolves fat and fat-like substances and, in this and other unknown ways, it affects protoplasm with which it remains in contact, for even a short time, with the following results: It causes local irritation, this, when the drug is taken by mouth or inhalation, includes the mucous membrane of the alimentary canal and, in the latter form of administration, the respiratory tract. It irritates the organs through which it is excreted (lungs and kidneys); and sometimes the heart muscle. If taken in large enough amounts it depresses nerve centers, some more readily than others, so that, the depression occurs in the following order: First the psychic centers, and their intellectual and inhibitory faculties are primarily affected; next the sensory centers; then the cerebral motor and the spinal reflex centers; the medullary centers are affected last and to the

least extent; in fact, these centers, as a rule, if the ether is properly administered, show few, if any, signs of depression and there is evidence of at least a temporary stimulation. Whether this stimulation is due to direct irritation of the centers by the ether or to reflexes induced by the irritation of the mucous membrane, is not known. The vasodilator centers supplying the skin and the sweat centers are apparently stimulated throughout the anesthesia, as the result of the local irritation.

Ether tends to disintegrate red-blood corpuscles by abstracting their fat, but the amount generally absorbed during anesthesia is not sufficient to do this to a harmful degree.

When small amounts are taken by mouth, the effects of its local action are practically the only ones observed.

Ether has a slight depressant action on the protoplasm of bacteria.

Effects of Actions:

Ether is an antiseptic and, because of its action on fat, a good detergent.

If ether is applied to the skin and allowed to evaporate it will, by abstracting heat, cool it and, as cold depresses protoplasm and thereby lessens the sensitiveness of nerve-endings, ether has a slight local anesthetic effect. But, as ether causes irritation of tissue with which it remains in contact, if it is applied to the skin and covered, so that its immediate escape is hindered, it has the effects of a rubefacient counterirritant, described page 57.

When a small amount of ether is given by mouth the stimulation of the nerve-endings of taste and smell increases the secretion of saliva, while the irritation of the mucous membrane, increases the amount of blood in the membrane and gives rise to reflexes that have both local and systemic effects. **The local effects** are increased secretion of mucus and contraction of the muscle tissue of the alimentary canal. As the result of the contraction of the muscle tissue, gas may be expelled from the stomach and intestine and, if a large, but not anesthetic, amount

of ether is taken, it may cause vomiting. **The systemic effects** are due chiefly to reflex stimulation of the respiratory, vasoconstrictor, vasodilator, and cardiac accelerator centers, and, possible psychic centers. As is typical of reflex stimulation, the effects are instantaneous, but transitory. They are: Increase in the rate and depth of breathing, and in the rate and force of the heart action; a slight rise of blood pressure, due to the effect on the heart and the contraction of the deeper arteries; a slight dilation of some of the skin-vessels. These effects may help to overcome faintness. The stimulation of psychic centers may possibly increase their inhibitory power sufficiently to help a person control an inclination to give way to emotion.

The heart muscle may be temporarily stimulated by a small amount of ether after its absorption but, otherwise it is not as a rule directly affected to any extent, except by poisonous doses or prolonged anesthesia when it tends to be depressed.

When ether is given by inhalation in sufficient quantities to produce anesthesia, the irritation of the mucous membrane is excessive and, **until the centers are depressed,** the effects just described, except the stimulation of the higher cerebral centers, are very pronounced. The pychic centers are so quickly depressed by large amounts of ether that their primary reflex stimulation is not apparent. The results are as follows:

The **local congestion** of the mucous membrane of the throat involves the Eustachian tubes. This changes the circulation and the air pressure within the ears and tends to promote sensations of ringing, buzzing and dizziness.

The **excessive mucus** in the throat and the presence of the inhalation mask interfere with the free interchange of respiratory gases and thus a state of partial asphyxia is produced. This condition is likely to be increased, if the patient struggles, for the breathing will then be interfered with. The patient becomes cyanosed in proportion to the degree of asphyxia produced.

The **distress** occasioned by the irritation, congestion,

asphyxia and, sometimes, fear, cause very pronounced stimulation of sympathetic and other reflex centers with the following results: The rate and force of the heart action are increased. There is a decided rise of blood pressure, due to the effect on the heart and the contraction of the majority of blood-vessels. The vessels in the skin, however, are dilated and, therefore, the latter is flushed and, if properly protected, warm. Perspiration is profuse. The breathing, if not interrupted by the patient struggling, is quicker and deeper than usual. The pupils are dilated, due to the stimulation of the sympathetic nerve supplying the radial muscles of the irises. Muscle tone is increased.

The **partial depression of psychic centers** involves loss of memory, the power of self-control and ability to reason, and the patient is likely to become very excited and emotional and to cry, shout, laugh, sing, struggle. Consciousness is dulled at this stage but not entirely lost.

As soon as enough ether has been absorbed to produce unconsciousness the effects of reflex stimulation cease, because the nerve-centers are too depressed to respond to the stimuli coming in over the afferent fibers. **Breathing** becomes slower and more shallow though, normally, not more so than before the administration of the anesthetic was commenced. As more air and less ether is given at this stage, there is less asphyxia and thus little, or no, cyanosis. **Blood pressure and the rate of the pulse** also become about what they were previous to their stimulation. The **skin vessels** remain dilated, but **those of the kidney** may be constricted for some time, especially if there was a marked degree of asphyxia. **Perspiration** continues to be profuse. **Muscle tone** becomes diminished. The skeletal muscles, except those concerned with respiration (these continue to receive impulses from the respiratory center) are more affected than the plain muscle tissue. The tone of the muscle tissue of the iris is an exception, this, normally, is not diminished. The **pupils**, as excitement subsides, contract to the degree

that is usual in natural sleep. All **reflexes** that can be tested, except the response of the pupils to light, are abolished by the time that sensation is sufficiently dulled to allow cutting to be done without causing pain. The last reflex to be lost, with the exception of that just mentioned, is the response of the eyeball to pressure.

As the result of the depressed condition of the nervous system and muscular relaxation, **metabolism** is inhibited and this, and the excessive loss of heat (resulting from the extra amount of blood in the dilated skin vessels and the free perspiration) cause a decided reduction of **temperature.**

The extra loss of water from the blood through the sweat glands and the lessened amount of blood in the renal vessels (due to their contraction and to the unusual amount of blood in the skin vessels) inhibits the **secretion of urine.**

The kidney cells are sometimes harmfully affected. Whether this is due to their direct irritation by the ether or to the interference with their blood supply is not definitely known, but the latter is thought to be at least partly responsible, if the kidneys are thus affected there will be albumin and, sometimes, casts in the **urine.** Occasionally there is **acetone** in the urine for a day or two after operation, this indicates defective metabolism.

The various results of the peripheral irritation and the central depression that ether induces give rise to fairly distinct phases in the process of anesthetization. These are termed *the three stages of anesthetization* or, some authorities count the final condition of the third stage, that in which the operation is performed, as a fourth stage.

The first stage includes the period in which the patient is fully conscious of the distress occasioned by the conditions brought about by the irritation of the ether and the partial asphyxia, but, unless very nervous, is able to exert self control.

The second stage is the interval in which the effects of peripheral irritation and the stimulation of the sympathetic system (by distress, fear, etc.) and the depression

of the higher psychic powers are most marked. It is often termed the *stage of excitement*, because of the intense excitement and lack of self-control commonly exhibited, as described on page 103. The patient is still conscious during this stage, though consciousness is blunted and, apparently, the condition of the brain tissue does not allow the production of the unknown effects which constitute the formation of memories for, upon recovery from the anesthetic, the patient does not remember anything that occurs from the beginning of this stage until the effects of the ether upon the brain subside. This stage may last only a few minutes, but it is likely to be prolonged if the patient is nervous or addicted to the overuse of alcohol.

The third stage is considered to begin with the loss of consciousness and the cessation of the signs of stimulation, as described on page 103. Ordinarily, if the ether is properly administered and the patient is not in a serious condition, this stage can be maintained for an hour or two or even longer, without bad effects, but, if the depression of nerve-centers, especially those of the medulla, exceeds that described as normal in this stage, collapse is likely to follow.

When death occurs as the result of ether anesthesia it is nearly always due to depression of the respiratory center.

Symptoms of danger are: Slow, shallow, or irregular breathing, cyanosis, increasing rapidity and weakness of the pulse, dilation of the pupils without other symptoms of returning consciousness. This effect on the pupils indicates the depression of the nerve-centers controlling the muscles of the irises and it has been found that when these centers are depressed, fatal depression of the vital centers is imminent.

Treatment.—The anesthetic is discontinued and the head of the table lowered. Drugs which have the opposite action of ether on the brain and spinal cord—as caffeine, strychnine, and atropine—are generally given and, if necessary a saline infusion and artificial respiration.

Also, if the latter is necessary, the rectum is usually stretched by the introduction of a speculum, because this causes reflex stimulation of the respiratory center. It is particularly important that the patient be kept covered and warm during this treatment.

Prophylactic Measures.—Untoward effects are far more likely to occur if a patient is in poor health or weak from want of rest and food, or if the first and second stages of anesthetization are prolonged—the excitement in these stages by overstimulating the nerve-centers favors their subsequent depression. For these reasons, it is customary, if the patient is in poor health, unless an immediate operation is required, to postpone it until measures to build up the health have been tried. To prevent bad effects from lack of food, glucose is sometimes administered by rectum or intravenously and, to lessen acidosis from delayed metabolism, sodium bicarbonate may be given with it. To shorten the primary stages, morphine is commonly given and, to prevent the depressant action of the morphine on the respiratory center as well as to check the secretion of saliva and mucus, atropine or scopolamine is given with the morphine.

After the anesthetic is discontinued and the centers begin to regain their sensitiveness, conditions similar to those that occur in the second stage again become more or less evident. Also the patient is likely to be nauseated and the excessive amount of mucus, which is saturated with the irritant ether, is largely responsible for this as it falls into the stomach and acts as an emetic. The degree of excitement and nausea vary greatly in different individuals. They are likely to be greater in nervous people and when a large amount of ether has been given. If the patient is not disturbed by nausea, pain or excitement, he is likely to sleep the greater part of the time until the ether has been eliminated.

As the care that a patient requires before, during and after anesthesia is described in all text-books of nursing procedures, space will not be taken to discuss it here.

When ether is **administered by rectum** there will be the same inflow of impulses from the irritated membrane as when it is given by inhalation, but the choking sensations, ringing in the ears, etc., due to excess mucus and the congestion of the membrane in the throat will be lacking. The irritation of the intestinal membrane, however is apt to be very severe. When the ether is **given intravenously,** the reflex stimulation is lacking and anesthesia is produced in a few minutes.

CHLOROFORM

Chloroform is a colorless, non-inflammable, very volatile liquid. It is formed by the chemical interaction of alcohol and chloral. It has a sweetish, burning taste. It is readily decomposed by light and thus must be kept in dark colored bottles.

Preparations and Dosage:

For external use:

Chloroform liniment, this consists of chloroform 30 per cent. and soap liniment 70 per cent.

For internal administration:

Chloroform, 3–10 m. (0.2–0.6 c.c.).

Emulsion of chloroform, ½–1 ʒ (2.0–4.0 c.c.).

Spirits of chloroform, ½–1 ʒ (2.0–4.0 c.c.).

Chloroform water, 2–4 ʒ (8.0–15.0 c.c.).

Comparison of the Effects of Chloroform with Those of Ether.—With the exceptions here mentioned the actions of chloroform are similar to those of ether:

1. Chloroform is more irritant than ether. It is a general protoplasmic poison and, if concentrated, will destroy any tissue with which it remains in contact. If it is dropped on the **skin** and its evaporation interfered with, it is likely to cause blistering. For this reason the skin of the face is protected with vaseline or similar substance before giving chloroform inhalations.

2. The destructive action of chloroform on bacteria is much greater than that of ether. Chloroform is antiseptic

in solutions as dilute as ½ per cent. Its irritant and volatile properties, however, limits its use as a disinfectant.

3. Chloroform does not evaporate as quickly as ether and thus it does not chill the skin to the same extent nor does it act as a local anesthetic.

4. Chloroform in concentrations above 0.5 per cent. will inhibit the action of enzymes, including those which aid digestion and metabolism. In concentrations below 0.5 per cent., however, it aids the action of rennin and pepsin.

5. Though chloroform is more irritant than ether to mucous membranes, so much less is used to promote anesthesia, and so much more air is given with it, its irritant action on the mucous membrane of the respiratory tract and alimentary canal is less marked. Therefore, it causes less hypersecretion of saliva and mucus; less asphyxia and the conditions that asphyxia promotes, especially cyanosis and diaphoresis; also, nausea and vomiting are not as likely to occur.

6. Chloroform promotes anesthesia more rapidly than ether; its depressant action on the cerebrum being 3 to 3½ times greater than the latter. Thus, the first and second stages of anesthesia are passed through more rapidly than when ether is used.

7. Chloroform has a much more depressant action on the heart muscle.

8. Chloroform after temporarily stimulating the vaso-constrictor center depresses it and thus reduces blood pressure. Because of this action and the effect on the heart muscle, the pulse, during chloroform anesthesia, is likely to be weak and slow and death from heart failure is not uncommon. Also the relaxed conditions of the blood-vessels limits the amount of blood sent to the skin and, consequently, it is pale.

9. Chloroform has a much more depressant effect upon the respiratory center and thus breathing is relatively slow and shallow during chloroform anesthesia.

10. Chloroform interferes with metabolism to a much greater degree than ether and it is more injurious to the

tissues. Therefore, following chloroform anesthesia, the urine is likely to contain products of imperfect oxidation as acetone, an increased amount of ammonia salts and a corresponding decrease of urea (which is a product of the decomposition of ammonia compounds resulting from the catabolism of proteins); also, as the result of the ill effects of chloroform on the liver, there may be bile and glucose in the urine; and, in consequence of injury to the kidneys, albumin and casts. The reason that there is glucose in the urine, is that the liver cannot store the glycogen as usual.

If too much chloroform is used, or if it is administered several times at short intervals, its injurious action on the tissues is likely to cause fatty degeneration of some or all of the internal organs and thus promote the conditions described in the paragraph on delayed chloroform poisoning.

Thus it can be seen that, though chloroform has some advantages over ether as an anesthetic, it has several serious disadvantages.

To summarize: Its advantages are: 1. Chloroform anesthesia is produced and recovered from more rapidly than ether.

2. There is practically no irritation of the bronchi, lungs and alimentary tract and thus there is less hypersecretion of saliva and mucus, less congestion of the mucous membrane, and, consequently, fewer unpleasant sensations, and less neasea and vomiting.

Its chief disadvantages are: 1. Its depressant action on the heart muscle and the vasoconstrictor and respiratory centers; 2. Its tendency to cause delayed chloroform poisoning.

Toxicology:

Sudden death from heart failure is not uncommon during chloroform anesthesia and it is particularly likely to occur during the first and second stages; because the weakened heart muscle is unable to stand the resistance offered to it by the primary contraction of the blood-vessels, that is caused by the temporary stimulation of the vasocon-

strictor center. In the third stage death may occur either as the result of the reduced blood pressure or paralysis of the respiratory center.

Death may occur almost without warning, but it is generally preceded by the following symptoms of poisoning: The pulse becomes slow and weak, the breathing slow and shallow, the skin assumes a bluish pallor; the pupils dilate widely.

The treatment for acute poisoning is the same as for that by ether and other depressant drugs, except that, as a rule, the patient's position (lowering the head) is not changed at first, because even this much disturbance is likely to precipitate collapse.

Delayed chloroform poisoning, as previously stated, is the result of the interference with metabolism in consequence of which the tissues of some or all of the internal organs become degenerated and there is an accumulation of the products of defective metabolism in the body

The symptoms, which may appear in a few hours or not for several days, are: Delirium alternating, as a rule, with periods of stupor. Continued vomiting with, possibly, after a time, blood in the vomitus. The pulse becomes slow and weak and the breathing slow and shallow and, consequently, there is marked cyanosis. There is a sweetish odor to the breath, due to the acetone in the blood. The urine is scanty and, generally, contains albumin, blood, casts (due to injury to the kidneys), acetone, diacetic acid, and other products of defective metabolism.

Collapse, followed by death, in from one to three days after the appearance of the symptoms is the usual result of this condition. It is rarely recovered from. It is more likely to occur in children than in adults, and anemia, diabetes, diseases of the kidneys or liver, and alcoholism are predisposing causes.

ETHYL CHLORID

Ethyl chlorid is an exceedingly volatile, inflammable gas that is prepared by the action of hydrochloric acid on

alcohol. It can be condensed (and thus made liquid) at a temperature of 55.4°F. and, if kept under pressure, as in a sealed tube, it can be maintained in liquid form. As soon as the pressure is released, however, the ethyl chlorid (following the usual behavior of condensed gases) begins to volatilize. Heat is necessary for the volatilization and the ethyl chlorid takes what it requires from anything upon which it strikes. Therefore, if enough is sprayed upon any part of the body, it will freeze the area. This action will be further discussed in connection with local anesthetics, it is not made use of for general anesthesia.

When ethyl chlorid is used to induce general anesthesia, it is volatilized into an inhaler and the gas is then inhaled.

When it is inhaled, ethyl chlorid acts in very much the same manner as chloroform, but it causes general anesthesia more rapidly than the latter (in 1–2 minutes). It does not, however, cause as complete muscular relaxation and it depresses the heart to an even greater degree. Because of the two last actions, ethyl chlorid is rarely used as a general anesthetic, except for short operations that do not require muscular relaxation and as a preliminary to ether anesthesia.

ETHYL BROMIDE

The action of ethyl bromide is similar to that of ethyl chlorid but it is not so volatile and it does not produce anesthesia as quickly as the latter. It is very seldom used.

PENTAL

Pental is prepared from fusel oil. It produces anesthesia very quickly and it does not affect the heart or respiration, but it does not depress the motor centers to the degree that ether and chloroform do and therefore muscular relaxation is very incomplete and muscular twitching, and even convulsions, may occur, thus it is rarely used.

NITROUS OXID GAS (N_2O)

Nitrous oxide gas is much more frequently used as a general anesthetic than the three drugs last mentioned, but it is placed after them because it does not, like them, belong to the same chemical group as ether and chloroform.

It is prepared by the distillation of salts of ammonium nitrate (NH_4NO_3) as the gas (nitrous oxid) is evolved it is collected in steel cylinders.

Action.—Nitrous oxid has no local action. After absorption it depresses the central nervous system, especially the psychic and sensory centers. It has very little effect upon motor centers. While it is in the blood it inhibits the combination of oxygen with hemoglobin and thus, even when it is given with oxygen, it tends to promote more or less asphyxia and the other effects of nitrous oxid anesthesia are due to the asphyxia, and not to the direct action of the drug. The conditions and results of asphyxia are discussed on page 96.

Nitrous oxid depresses the psychic and sensory centers even more rapidly than chloroform, in about 2 or 3 minutes. The depression of the psychic centers occurs in the usual gradation, as described under ether.

Nitrous oxid is eliminated through the lungs very rapidly. There will not be enough left in the blood to continue the effects upon the nervous system 3 or 4 minutes after its administration is discontinued.

Effects of Action.—The patient is likely to be emotional and to talk and laugh for a minute or two. At the end of this time sensation and consciousness are lost, but muscular relaxation is very incomplete.

As the result of the asphyxia, the **pulse** will be relatively slow and strong, the **blood-pressure** high, the **breathing** deep and stertorous; and the **color** flushed and somewhat cyanotic.

The changes in the blood pressure and the breathing affect the circulation and the air pressure in the ears

are thus probably responsible for the ringing and other noises that the patient generally hears before losing consciousness.

Uses.—Nitrous oxid in combination with oxygen is now much used in obstetrical work and for short operations in which muscular relaxation is not necessary, and as a preliminary to ether anesthesia.

It is generally considered that, if this combination is properly given, it is about the safest anesthetic that can be used, provided its use is not continued too long—much above ½ hour.

The people who are most easily **detrimentally affected** by it are: Young children, in whom asphyxia is very easily produced; people with high blood pressure, heart lesions or arteriosclerosis.

Danger signals are increasing cyanosis and high blood pressure (indicated by slow, forceful pulse), dyspnea and, sometimes, if the premonitory symptoms are not observed, convulsions. These symptoms are due to the asphyxia and will as a rule disappear as soon as the inhaler is removed.

MAGNESIUM SULPHATE (EPSOM SALT)

This salt is very commonly found in springs and salt deposits.

Dosage.—For *intravenous administration* a 6 per cent. solution is generally used; for *subcutaneous and intraspinal injections*, and for *injection into nerve-trunks*, a 25 per cent. solution is commonly employed. The amount used depends upon the object of the administration. The maximum dose, to prevent convulsions, is about for adults 1.2 c.c. for each 20 pounds of body weight; and for children 0.5 c.c. for each 20 pounds. For **external use, a** saturated solution (15 per cent.) is employed. The dosage for *use by mouth* is given in the section on Cathartics.

Actions.—When magnesium sulphate is administered by mouth it does not, as a rule, have any effect upon the

nervous system because, as it is slowly absorbed from the intestine and readily excreted by the kidneys, unless it is taken in poisonous amounts, there is not sufficient accumulation in the blood. Its action when administered by mouth will be found in the section on Cathartics.

If a saturated solution of magnesium sulphate is kept in contact with a part, especially **raw tissue**, it will act as an astringent (described on page 47) and it lessens the sensitiveness of nerve-endings in the area.

Magnesium sulphate depresses both sensory and motor **nerve-endings** with which it comes in contact, but the former to a greater degree than the latter. If magnesium sulphate is injected into a **nerve-trunk**, its action upon the fibers will prevent the passage of impulses. When it is given **intravenously** and **intraspinally** it acts chiefly upon the synapses of neurones, more especially afferent neurones, with which it comes in contact. Thus its action on nerve centers is the opposite of that of strychnine.

Effects of Action.—As the result of its action on sensory nerve-endings magnesium sulphate either when applied externally or injected subcutaneously, will lessen pain and, when saturated solutions are kept in contact with abraded surfaces, there will also be some shrinking and drying of the tissue from the salt action. Also, when injected into a nerve, magnesium sulphate lessens pain.

As the result of its action on the synapses, magnesium sulphate blocks the passage of impulses through the centers and thus it prevents consciousness of pain and lessens muscular contractions (which are due to impulses discharged from nerve centers) and, in large enough doses, it checks convulsions. In still larger doses, it produces a general anesthesia resembling that of chloroform, but in such doses the interference with the passage of impulses in the cord is likely to inhibit breathing.

When it is given intraspinally, the effects will last for from 24 to 48 hours.

The chief therapeutic uses of magnesium sulphate by the methods of administration described here are:

As a local external application to lessen pain in dermatitis, burns, cellulitis, ulcers and the like.

Injected into a nerve to lessen pain such as that due to neuralgia and sciatica.

Intraspinal or intravenous injections are used to prevent convulsions, especially those due to tetanus and strychnine poisoning. The former are sometimes used to block the passage of afferent impulses through the cord and thus promote anesthesia in parts of the body supplied with nerve fibers that enter the cord below the site of injection.

Untoward effects are the result of interference with breathing and the symptoms are those of asphyxia.

The **treatment for poisoning consists** in giving artificial respiration until breathing is resumed. Drugs which have the opposite action, strychnine, physostigmine and caffeine are likely to be prescribed and an intravenous injection of calcium chlorid 2.5 per cent. is given. Calcium chlorid has an affinity for the same structures (the synapses) that the magnesium sulphate effects and will displace the magnesium. It is customary, when a large dose of magnesium sulphate is to be used, to prepare a solution of calcium chlorid that may be ready in case of emergency.

ALCOHOL

Ethyl alcohol is **prepared** by fermenting sugar solutions with yeast. The sugar solution may be that of fruit juices or it may be derived from starch by its preliminary fermentation with yeast or with a ferment known as *diastase of malt.*

There are a number of alcohols, but ethyl alcohol is the only one used as a beverage. It is employed for this purpose in the form of wines and similar liquors, which contain some of the other ingredients of the solutions fermented to produce the alcohol.

Fermentation will not yield a liquor with more than about 15 per cent. alcohol, because higher per cents. than this

kill the yeast. Thus, alcohol and what are known as *distilled liquors* are obtained by distilling the fermented material, and wines with a higher percentage, have alcohol added to them and are therefore known as *fortified wines.*

In the **preparation of distilled liquors,** water and volatile substances are allowed to remain in the distillate, but, for pure alcohol, these substances are removed as far as possible.

Alcohol is Sold in Three Strengths.—Absolute alcohol which is 99 per cent. (by volume); alcohol, 95 per cent. dilute alcohol, 50 per cent. **Denatured alcohol** is ethyl alcohol plus some substance, such as wood alcohol, or other poison, which renders it unfit for drinking. It is tax-free and therefore, cheaper than pure alcohol.

Alcoholic beverages are usually **classified as: Malt** liquors, wines, distilled liquors, liqueurs.

Malt liquors include beers, ales, porter and stout. **They are made** from grains which are prepared for fermentation by preliminary exposure to the action of diastase of malt (a ferment prepared from barley). **They contain** alcohol, 3–10 per cent., starches and sugars, and also extractive matter from hops which gives them a bitter flavor and a slight narcotic effect. In cheap beers, bitter substances, such as gentian and quassia, are often substituted for the hops.

Wines are classed, according to their color, as white and red; those with sugar, as sweet wines; those with little or no sugar, as dry wines; those containing carbon dioxid as sparkling wines; those with more than 15 per cent. alcohol as fortified wines.

The white wines are made by fermenting the juice and pulp of grapes; they **contain,** as a rule, from 7–12 per cent. alcohol. **Champagnes** are white, sparkling wines. They contain about 10–15 per cent. alcohol and, as stated above, carbon dioxid, which increases their carminative properties.

Red wines are made by fermenting the whole grape, including skins and seeds. As there is tannin in these

substances, red wines are somewhat astringent. The clarets and non-fortified red wines contain about the same amount of alcohol as the white wines but **port wine** contains about 20–40 per cent. alcohol; **sherry**, 15–20 per cent. and some of the **burgundies** and other sweet red wines contain as much as 20 per cent. alcohol.

The usual dose of the wines is 1 wine glass full. Champagne, when used to relieve nausea, is given in dram doses, at short intervals, and the bottle must be kept tightly corked, and upside down, on ice, so as to avoid loss by carbon dioxid.

The distilled liquors are:

1. Whiskey (*Spiritus frumenti*)
   - American, made by distilling fermented rye, corn or wheat.
   - Scotch, made by distilling barley.
   - Irish, made by distilling fermented potatoes.

Whiskey contains from 45–55 per cent. alcohol. It should not be used until at least four years old as, while fresh, it is too irritating to the tissues. The flavor is also improved by age.

2. Brandy or cognac (*Spiritus vini gallici*), this is made by distilling fermented grape juice. It contains about the same percentage of alcohol as whiskey and, like whiskey, it should not be used until it is at least four years old. Brandy also contains tannic acid and thus has a slight astringent action on the mucous membrane of the stomach and intestine and promotes constipation.

So called brandies are also made by distilling fermented juices of fruits other than grapes. These are known by the name of the fruit from which they have been prepared, *e.g.*, blackberry brandy, peach brandy. Their alcohol percentage varies greatly.

3. Rum, this is the distillate of fermented molasses. It contains about the same amount of alcohol as whiskey.

4. Gin, this is the distillate of fermented rye mash redistilled with juniper berries. Gin contains about

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ETHYL

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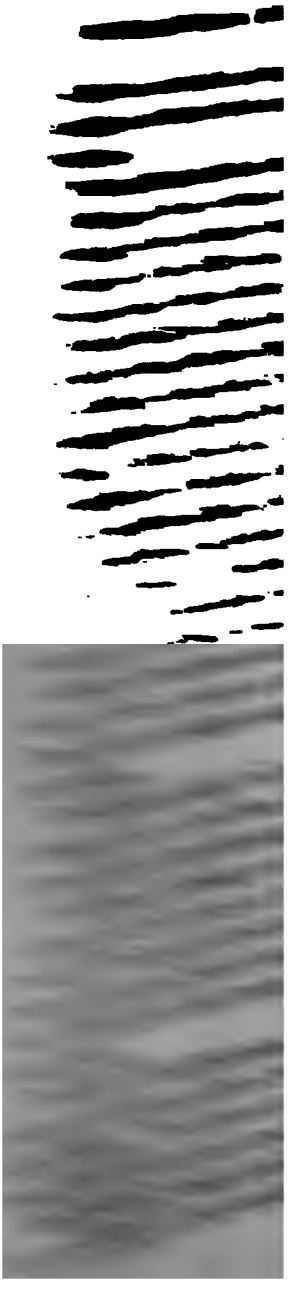

60–70 per cent. alcohol and, usually, some oil of juniper, which gives it diuretic effects and adds to its carminative properties.

The usual therapeutic dose of the liquors is ½ ounce.

Liqueurs, known as cordials and elixirs, are syrups containing various aromatic substances and alcohol in amounts of from 50–70 per cents. Examples are: Chartreuse, absinthe, crême de menthe.

Fate in the Body.—Alcohol is not absorbed through the skin, but it is readily absorbed through mucous membranes and, if taken by mouth while the stomach is empty, the systemic effects of a dose will be observed in about 20–25 minutes. When there is food in the stomach, however, the absorption of the alcohol is retarded. After absorption, alcohol passes through the portal vein to the liver and from thence into the general circulation. Between 90 and 95 per cent. of the alcohol absorbed is oxidized in the body to carbon dioxid and water, the remainder is eliminated in the breath, urine and perspiration.

Actions.—Alcohol abstracts water from protoplasm with which it comes in contact and coagulates its protein. Thus, it acts as an astringent causing shrinking of tissues and irritation.

If **the irritation** is slight, it will, as usual, have a mild stimulant action on most tissues, but, if severe, it will depress them and cause inflammatory changes.

Hard tissues, like **the skin,** are not as much affected by alcohol as the softer ones and, as alcohol evaporates readily, if it is applied to the skin and left uncovered, it passes away so quickly that it does not induce irritation, but it takes the heat that it requires for its evaporation from the skin.

The action of alcohol upon **mucous membranes** is very marked and solutions as dilute as 2 per cent. will produce slight irritation. This is the case also with **subcutaneous tissues** when alcohol is given by hypodermic.

When it is taken by mouth, alcohol stimulates the olfactory nerve-endings and some taste-buds and it irritates

the membrane of the mouth, throat, esophagus and stomach but, unless large doses are taken, the membrane of the intestine is not likely to be irritated because a considerable portion of the alcohol is absorbed through the stomach and the remainder is diluted by the gastric and intestinal contents.

The actions of alcohol after absorption are so modified by the reflexes induced by the irritation of the mucous membrane that its nature has been much disputed, but it is now generally believed that, possibly after a very transitory stimulation, **nerve-centers** are depressed, the higher psychic centers first and to the greatest degree; also, apparently, either the vasoconstrictor center supplying the vessels in the skin is depressed very quickly or else vasodilator centers are stimulated, and there is evidence of slight stimulation of the respiratory center, but some authorities believe that these results are not due to the direct action of the alcohol. Small doses may, some authorities think, stimulate the heart muscle but large doses depress it. Large amounts apparently irritate the kidneys and the immoderate use of alcohol for an extended period may produce a nephritis and also injure the tissue of other organs, especially the blood-vessels, heart and liver.

In its actions before absorption it is the **concentration** rather than the amount of alcohol that is of importance; *e.g.*, one ounce of a beverage containing 20 per cent. alcohol will have a much stronger effect upon the gastric mucous membrane than 10 ounces of a 2 per cent. beverage; but, as the concentration of alcohol in the blood will be in proportion to the quantity absorbed, the amount of alcohol taken is of as much importance as the concentration of a beverage in the production of effects after absorption.

In considering the effects of the concentration of beverages, it is necessary to make allowance for the stomach's contents; *e.g.*, a 20 per cent. beverage taken with a meal will probably not have any more effect than a

2 per cent. one taken when the stomach is empty. Food in the stomach also retards the absorption of alcohol and thus the systemic effects of a beverage are not as pronounced when it is taken with, or shortly after, a meal as when the stomach is empty.

As previously stated, alcohol is, ordinarily, only used internally in the form of wines, liquors, etc. and, in considering the effects of these, their other ingredients must be taken into account. The most important ones are: (1) The tannin in red wines and brandy, which, because of its astringency, retards digestion and absorption and promotes constipation; (2) the extractive matter in malt beverages, which also tends to retard digestion; (3) the bitter principle in malt beverages and the aromatic substances in wines and liquors, which stimulate the appetite and the secretion of saliva and gastric juice and thus aid digestion; (3) the sugars in malt beverages and sweet wines, which sometimes undergo fermentation and cause flatulence; (4) the carbon dioxid in sparkling wines, which has a carminative action.

Effects of Actions.—As alcohol has the same astringent effect upon the protoplasm of **bacteria** that it has upon human tissue, it, in concentrations between 50 and 70 per cent., is a disinfectant; between 15 and 50 and above 70 per cent. it is antiseptic. Its lessened power to destroy bacteria in the higher percentages is due to the rapidity with which it coagulates the superficial protein of the organisms, for the coagulum thus formed inhibits the penetration of the alcohol to their vital tissue.

When alcohol is applied to the **skin** and the part covered, it produces sufficient irritation to act as a rubefacient, as described under counterirritation. If the skin is left uncovered so that the alcohol can evaporate readily, the only effect of the latter's action on protoplasm will be a slight drying and hardening of the skin, but, as the alcohol takes the heat that it requires to further its evaporation from the skin, it cools it and thus stimulates the nerve-endings in it that respond to cold. This, if a large

area of skin is involved, as in an alcohol bath, produces the usual physiologic reactions to cold.

The results of the irritant action of alcohol on mucous membranes are: (1) Increased secretion of mucus; (2) dilation of the blood-vessels in the part with a consequent sensation of warmth and well-being; (3) if the irritation is at least moderately strong (as that produced by a 20 per cent. beverage, taken while the stomach is empty) reflexes are produced that (*a*) promote peristalsis and thus aid in the expulsion of gas; (*b*) stimulate the medullary centers, especially the respiratory, vasoconstrictor and cardiac accelerator centers; and it is thought that the dilation of the skin blood-vessels that follows the use of even small doses of alcohol may be partly due to reflexes. Excessive irritation, especially if frequently repeated, will cause inflammation of the mucous membrane and the secretion of a thick tenacious mucus.

Results of the Action of Alcohol on Digestion.—The secretion of saliva and gastric juice is increased and also the hydrochloric acid of the gastric juice; thus the latter is unusually acid after the use of alcohol. As the result of this it is thought the pancreas receives extra stimulus, because, it will be remembered, acid entering the intestine is supposed to change a substance, known as *prosecretin*, which is manufactured by intestinal glands, to a hormone—secretin—which, when carried by the blood to the pancreas, activates it. Beverages containing about 2 per cent. alcohol, or if reduced to this in the stomach, increase the activity of the pepsin, those with concentrations between 5 and 10 per cent. have almost no effect upon the **digestive ferments**; those with higher concentrations inhibit the activity of the ferments.

Beverages with less than 10 per cent. alcohol have practically no effect upon the **food material in the stomach,** but alcohol in higher concentrations coagulates the protein of food.

Thus the alcohol in beverages, if diluted to between 2 and 10 per cent., favors digestion and (because of the

extra amount of blood in the alimentary mucous membrane) absorption, but higher concentrations retard digestion.

As, however, alcohol makes the gastric juice unusually acid, alcoholic beverages will be harmful when a person has hyperchlorhydria (excessive secretion of hydrochloric acid) gastric ulcer, or gastritis.

Effects of Alcohol on the Nervous System.—In addition to the transitory reflex stimulation, induced by the irritation of the mucous membranes, there may possibly be an even more transient stimulation of nerve-centers induced by the direct irritant action of alcohol after absorption, but the almost immediate effect is that of depression the degree of which will depend upon the amount of alcohol taken and the individual's tolerance for alcohol. As previously stated, the psychic centers are most easily affected and the medullary centers least. Of the medullary centers, the vagus supply for the heart is apparently the first depressed.

As the result of moderate amounts of alcohol upon **psychic centers,** intellectual activities that require concentration of attention are inhibited, but the activity of the imagination may be increased. This is particularly likely to be the case with people, such as writers and inventors, who are used to exercising this faculty. The increased action of the imagination, however, is not due to stimulation, but to the inhibition of activities which interfere with its freedom. The ideas conceived while under the influence of alcohol can seldom be properly expressed or systematized (because of inability to concentrate the attention) until the effects of the alcohol have subsided.

The depression of the psychic centers also tends to lessen any propensity to worry or grieve or to indulge in introspection.) It lessens self-consciousness and nervousness and it increases confidence in one's capacities; for these reasons, drinking a small amount of an alcoholic beverage makes it easier for some people to speak, play or sing in public. It was largely because of this that, until recently,

alcohol in a small amount was considered a cerebral stimulant, but, as a matter of fact, if a person is in quiet surroundings, even a small amount of alcohol acts as a sedative.

When a moderate quantity of alcohol is taken in the midst of gay surroundings, the lights, music, and other stimuli will induce exhilaration, and the drinkers are likely to behave in much the same manner as excited children, for it is the faculties that have been acquired since childhood that are depressed.

Larger amounts of alcohol will so depress the **psychic centers** that power of self-control is lost and the person is likely to become very emotional or quarrelsome, gross and sensual. Such a condition is likely to be followed by narcosis.

The depression of the **reflex centers** and the **cerebellum**, that follows the use of large amounts of alcohol, reduces muscular contraction and prevents muscular coördination, thus the individual staggers when walking and sometimes cannot even hold anything. The lessened muscular contraction, by reducing the tension at which the bones are held, lessens the tendency to fractures from falls and blows.

The rate of **breathing** is increased. The cause of this is not definitely known, for experiments do not seem to show any increase in the sensitiveness of the respiratory center to stimuli.

The effect of moderate doses of alcohol on the **circulation** is not at all pronounced. As previously stated, the irritation of mucous membrane causes a slight reflex stimulation of the cardiac accelerator and vasoconstrictor centers and this causes a transitory increase in the rate and strength of the pulse and a temporary rise of blood pressure. After the alcohol has been absorbed it has a very slight direct stimulant effect upon the heart muscle[1] and this, with the

[1] The action of alcohol upon the heart has been a much debated question; at one time, it was thought to be a strong stimulant, then it was said to have no stimulant action whatever, but the theory given above seems to be the common one at present.

at the surface of the body) lessen congestion caused by exposure of the body to cold, and thus, by reducing conditions that are favorable for infection, check a cold.

To prevent the local effects of carbolic acid in poisoning. The mixture must be removed from the stomach immediately, for the alcohol hastens the absorption of the carbolic.

Toxicology.—The symptoms of acute alcohol poisoning are usually classed in two stages, viz., the stage of excitement and the stage of stupor.

In the stage of excitement the individual is excitable and emotional, ready to cry and laugh for little or no cause, he is often talkative and boisterous, but, sometimes, morose, sullen, and quarrelsome. His speech is thick and incoherent and his gait staggering. His muscles are relaxed. His skin, especially that of his face, is red and moist. His breathing and pulse are rapid.

In the second stage, the intoxicated person passes into a state of narcosis from which it is difficult to arouse him. His breathing becomes slow and stertorous and, consequently, his color grows cyanotic. If a fatal amount of alcohol has been taken, unless antidotal treatment is effectual, the narcosis becomes profound and merges into coma, collapse and death.

The treatment for acute poisoning depends upon the severity of the condition. If the pulse and breathing do not indicate danger all that is usually done is to lavage the stomach (this may be omitted if the patient vomits profusely and a fatal amount of alcohol has not been taken), provide warmth and fresh air, and let the individual sleep. If the pulse becomes weaker or the breathing dyspneic, stimulants such as caffeine, hot coffee, and strychnine are usually prescribed.

The symptoms of chronic poisoning (*alcoholism*) are: Mental deterioration with lack of energy, self-control, will power and memory. Nervous manifestations such as irritability of temper, tremor of the muscles, especially those of the fingers, lips and tongue; disturbed sensation,

this may be either hyper or hypo acute; insomnia; delirium; also, neuritis is common. Digestive disturbances (these are likely to be exceptionally severe because of the injury to the gastric membrane), constipation and, consequently, coated tongue and foul breath. A mottled appearance of the skin, especially that of the face, and purple lines, particularly on the nose and cheeks; both of these conditions are the result of permanently relaxed veins, the relaxation being due to their frequent dilation.

The delirium of alcoholism, known as **delirium tremens**, is a form of insanity, characterized by hallucinations of sight, hearing, and sensations that fill the individual with fear and horror. It is most likely to occur when an alcohol habitué is suddenly deprived of alcohol or subjected to unusual strain, such as is occasioned by the shock of an accident, or a surgical operation, or the sudden onset of disease, especially pneumonia.

The premonitory symptoms of an attack are: Growing restlessness, picking at the bed covers, nervous tremors, muttering, and the patient may call for protection from people, animals, snakes, etc. that he imagines he sees coming to attack him.

Unless the patient is quieted, these symptoms will be followed by violent delirium, in which he will shriek and struggle in terror and try to get out of bed, in order to escape from his vision enemies, and if opposed, he is likely to become exceedingly violent.

It is very important that the early symptoms be recognized, because if the patient is given a dose of whiskey or other alcoholic beverage, and an hypnotic, the threatened attack may be aborted.

The treatment of alcohol habitués, as far as the nursing care is concerned, is practically the same as that of those addicted to the use of other narcotics; viz.: To try to keep the patient amused or engaged in some interesting occupation, to maintain unceasing vigilance in order to prevent him getting alcohol, except that ordered by the physician; to do everything that will increase his strength,

this necessitates special attention to the diet, for the condition of the patient's stomach makes it difficult to give him as much food as he should have.

The drugs and special procedures used by different physicians vary, but an essential item in all treatments is the stimulation of elimination and thus cathartics and, sometimes, diuretics and diaphoretics are used liberally.

METHYL (WOOD) ALCOHOL

Methyl or wood alcohol is made by the destructive distillation of wood. It is not used in therapeutics for it is very poisonous. It is, however, a very common cause of poisoning, because, as it is employed in a number of industries, it is easily obtained and it is cheaper than ethyl alcohol. Its action upon protoplasm is the same, as that of ethyl alcohol, but much more pronounced, and an amount of methyl alcohol, that would be a moderate dose of the ethyl will cause nausea, vomiting, delirium, and, sometimes, death or, if the patient recovers, blindness is likely to follow, due to the destruction of some part of the optic nerve, and there may be various other abnormal conditions due to injury to the tissues of the organs involved.

HYPNOTICS OR SOPORIFICS

As previously stated, hypnotics or soporifics are drugs that induce a state of unconsciousness (termed hypnosis) that resembles sleep.

SLEEP, INSOMNIA AND HYPNOSIS

Sleep has been defined as *"that condition of inactivity of the parts of the brain associated with consciousness which follows the withdrawal of excitory stimuli,"* and consciousness, as *"a compound of intellectual action and sensation."*

The withdrawal of excitory stimuli is partly voluntary and partly a physiological process.

The usual voluntary means of lessening stimuli are: Retiring to a quiet and darkened room, relaxing the muscles by lying down in a comfortable position; ceasing to

think, at least of anything exciting or that requires attention.

The primary cause of the **physiological lessening of cerebral stimulation** is undecided. One theory is that the condition in the cerebrum, whatever it may be, is at least partly brought about by the so-called fatigue poisons (acids, etc. produced as the result of activity). Some of the physiologists who believe this theory consider that the toxins act by lessening the irritability of nerve-cells so that the latter do not respond readily to stimuli, and others think it possible that the toxins cause some change in the synapses of the neurones, which interferes with the passage of nerve-impulses. Another theory is that sleep is induced by fatigue of the cells resulting from their own activity.

Condition During Sleep.—The muscles are somewhat relaxed; the amount of blood in the limbs is increased and that in the brain diminished; the breathing is relatively slow and shallow; consciousness is more depressed than other nervous functions and stimulation of sensory nerve-endings will, without waking the individual, induce reflexes and, sometimes, stimulate subconscious activity and thus cause dreams.

Whatever may be the cause of **sleep,** lessening sensory impulses is, except in cases of extreme fatigue, an **essential** and anything that arouses cerebral stimulation, *e.g.*, pain, discomfort of any kind, mental excitement, especially that due to unpleasant experiences, is likely to prevent it. It is said that insomniphobia (fear of not sleeping) is one of the most common causes of insomnia for it causes the maintenance of mental tension and restlessness which are antagonistic to the muscular relaxation that promotes the conditions conductive to sleep

Hypnosis[1] is not true sleep, but is a condition of unconsciousness promoted, it is thought by some chemical or physical change in the protoplasm of the cerebral cells.

[1] From the Greek *hypnos* = sleep. The term is also used for the state of unconsciousness induced by suggestion, *i.e.*, hypnotism.

The main fundamental difference between the anesthetics and hypnotics is that the latter are so volatile that they leave the system quickly and thus can be used in greater concentration and to produce a deeper narcosis than it would be safe to induce with a less volatile substance.

Some drugs that produce hypnosis act directly upon the psychic centers of the association areas, but others act upon the sensory areas and, by depressing these, prevent the stimulation of the association areas, which, it will be remembered, receive all their stimuli through the cerebral sensory areas. Drugs which act in this way are analgesics, as well as hypnotics.

After the hypnotic is removed from contact with the cerebral cells by the blood, the conditions of sleep may exist for some time and, during the period, the cerebral cells will have a chance to repair the damage done to them by the drug. Unless they are thus recuperated, the individual, on awakening, will be exceedingly depressed, drowsy and tired. Even when the cells do have a chance to recover from the effects of the drug the individual is not likely to feel as refreshed as by natural sleep.

Hypnotics, by their action on nerve protoplasm, **if constantly used,** will interfere with the functioning of the nervous system. The higher capacities of the psychic centers—*e.g.*, the powers of reasoning, of self-control, the formation of memories—will be diminished; the reflex centers will be depressed and, thereby, muscle tone and secretion lessened. Consequently the function of all the body organs may be interfered with. There may be digestive disturbances and constipation with resultant coated tongue and foul breath, headache, faulty nutrition and, consequent, emaciation and anemia.

Some drugs, especially alcohol, opium and cocaine have, apparently, a more deleterious effect upon psychic centers than other drugs and are likely, if they are taken constantly, to so reduce the individual's will-power and moral sense that it becomes almost impossible for him to stop the use of the drug.

The use of hypnotics during illness is probably one of the most common causes for the formation of a "drug habit" and nurses should therefore do everything possible to induce a patient who is not in severe pain or suffering from an incurable disease to go to sleep without a hypnotic.

The main things to be considered in the treatment of insomnia are: (1) Everything necessary must be done to improve the patient's health so that (*a*) there may be no excuse for the use of a drug and (*b*) the condition of the cerebral tissue will be improved and thus better able to exert self control. (2) The patient should avoid excitement during the evening, this includes exciting plays and reading. (3) Tea and coffee should only be taken in small amounts, if at all, and not after luncheon. (4) The sleeping-room should be quiet, dark, cool, but not too cold, and well ventilated, though without draughts over the bed; the bed clothing should be sufficient to prevent the patient being cold but not enough to cause a sensation of warmth, nor heavy enough to promote discomfort. Heat, cold, discomfort of any kind will stimulate nerve-centers and thus induce conditions that may retard sleep. The patient should be warned that fear of not going to sleep or the belief that she will not sleep, will keep her awake. She should be instructed to lie quietly in a comfortable position and either to close her eyes or else to look fixedly at some one thing; to breath slowly, as is natural during sleep, to stop thinking and, sometimes, fixing the attention on a low monotonous sound, as the ticking of a clock that is at a distance, is a help. (6) Measures that tend to induce cerebral anemia are often of use, examples of these are, taking a light meal or even a glass of warm milk, before going to bed; lying quietly in a warm bath for about half an hour; this, especially if the bathroom is dark, will not only, by dilating the skin blood-vessels, lessen the amount of blood in the brain, but, by reducing the inflow of impulses to the nerve centers, act as a nerve sedative. (7) When there is no physical reason for a patient not sleeping an empty capsule or a hypodermic

injection of sterile water, that the patient believes to be a hypnotic, will often promote sleep quite as effectively as though it were and, if the substitute can be used for two or three nights with good results, there will be no better way of persuading the patient that a hypnotic is unnecessary. Of course, especially for the hypodermic injection, the doctor's permission should be had for the trial as it comes under the head of treatment.

The treatment for insomnia forms the basis of that for overcoming drug habits. Also constant watchfulness is necessary to prevent a habitué obtaining the "habit drug" and every possible endeavor must be made to interest such a patient in work or amusement.

CLASSIFICATION OF HYPNOTICS

Dr. Cushny classifies the majority of hypnotics under three headings, viz.: The chloral, bromide and opium groups.

The chloral group of hypnotics consists of compounds prepared from such substances as chlorine, alcohols, aldehydes, ethereal salts and certain acids. The drugs of this class contain somewhat similar chemical combinations to which their action on nerve-tissue is due and thus their effects are similar to those of chloral hydrate.

CHLORAL

Chloral is an oily, colorless liquid made by passing chlorine through absolute alcohol. Pure chloral is not used in medicine for it is very destructive to tissue and, unless otherwise stated, it is chloral hydrate that is meant when chloral is prescribed or its action discussed. Chloral hydrate, as its name implies, is made by the interaction of chloral and water.

Dosage.—Chloral hydrate 15–30 grs. (1–2 gm.). The dosage of other chloral compounds will be found with those of the other drugs belonging to this group on pages 136 to 139

Administration.—To avoid irritating the mucous membrane of the alimentary canal, it is well to dilute chloral hydrate with syrup. It should be given about 15–20 minutes before the time for sleep and after conditions have been secured that will allow of uninterrupted sleep.

Chloral should never be given with whiskey or other alcoholic beverage because the combination forms a substance that is exceedingly depressing to the brain. This mixture constitutes what is known as "knock-out drops."

Fate in the Body.—Chloral is readily absorbed from the stomach and intestines, its effects being apparent in about 20 minutes. The greater part of a dose is changed in the body to urochloric acid and, as such, excreted, chiefly through the kidneys, but a small amount may pass back into the stomach and be excreted in the feces. Its excretion is slow.

Actions:

Chloral is a general protoplasmic irritant poison. It affects the protoplasm of bacteria as well as that of animal tissues.

Applied to the **skin,** chloral acts as a counterirritant.

Unless it is properly diluted, chloral is very irritant to **mucous** membranes.

After **absorption,** chloral depresses **nerve-centers,** both those of the brain and cord. Therapeutic doses only induce a moderate degree of depression and have not much effect upon the medullary centers; except, apparently, the portion of the vasoconstrictor supplying the blood-vessels in the skin. Doses much above the maximum therapeutic dose, however, may promote a condition similar to chloroform anesthesia, but this is almost invariably followed by collapse.

Occasionally, the depression of the nerve-centers is preceded by a period of stimulation, comparable to the second stage of chloroform anesthesia. This, ordinarily, if it does occur, is very transitory.

After exerting a momentary stimulation (due to its irritant action) chloral depresses the **muscle tissue of the**

heart and blood-vessels. Except in susceptible individuals, the depression induced by therapeutic doses is slight, but amounts very little above the maximum therapeutic dose may induce intense depression.

Chloral, by its irritant action on tissue protoplasm, increases the destruction of protein, but, otherwise, it tends to interfere with **metabolism** in somewhat the same way as chloroform. The action of single therapeutic doses is not intense enough to be harmful but such interference with metabolism is sometimes one of the factors in producing the conditions of chronic chloral poisoning.

Effects of Actions:

Chloral is an antiseptic. When it is applied to the **skin,** chloral has the effects of a rubefacient (these are described in the section on counter-irritation) but, if a concentrated preparation is used in excess, it will act as a vesicant.

Unless chloral is well diluted, when it is given by **mouth,** its irritant action on the mucous membrane may cause nausea and vomiting.

After a therapeutic dose of **chloral has been absorbed** the patient becomes drowsy and, usually, soon passes into a condition resembling sleep in which the skeletal muscles are somewhat relaxed, the breathing is slower and more shallow, the pulse slower and rather weaker, and the skin blood-vessels are somewhat dilated so that the skin is flushed. Sensation becomes much less acute and thus the patient may not be disturbed by mild discomfort, slight noises and the like, but therapeutic doses of chloral do not depress the centers sufficiently to prevent their stimulation by acute pain, loud noises, and, other strong stimuli, and, therefore, such things may prevent sleep.

The extra amount of blood at the surface of the body favors loss of heat and the lessened metabolism (due to the direct action of the drug and to muscular relaxation) decreases heat production, thus the **temperature** is lowered.

Because of its depressant action on the **reflex centers of the cord,** chloral will lessen spasmodic contractions such as occur in convulsions.

If chloral is given during the first stage of labor it will relax the cervix without interfering to a marked extent with the rhythmical uterine contractions that occur during parturition.

Chloral is used to promote sleep, more especially when wakefulness is due to intense excitement or extreme nervousness, and during the first stage of labor, when this is prolonged; also it is used to prevent or check convulsions.

Due to idiosyncrasy, unusual effects sometimes follow even moderate therapeutic doses of chloral. The most common ones being: Excitement that resembles alcohol intoxication, this may persist for a considerable time and it may, or may not, be followed by sleep; headache; nausea; vomiting; extreme flushing of the skin and, sometimes, a rash; such extreme depression of the heart and nerve-centers that the pulse becomes exceedingly slow, weak and irregular, the breathing slow and shallow; and, unless the condition is relieved, collapse may occur.

Toxicology:

Symptoms of acute poisoning are: The breathing becomes very slow and shallow; the pulse weak, slow and irregular; the muscles extremely relaxed; sensibility to pain, as well as consciousness, is lost; the pupils are somewhat contracted; the temperature is subnormal.

The treatment is the same as for other depressant drugs. There is no chemical antidote. The special physiological antidotes are: Atropine, caffeine, strong coffee, strychnine, camphor. An enteroclysis or intravenous infusion of saline solution is commonly given, both to stimulate the circulation and to hasten the elimination of the drug. Artificial respiration is given if necessary.

It is particularly important to keep the patient quiet, not only during the first-aid treatment, but until the pulse shows that the effects of the drug on the heart action have ceased; for poisonous doses of chloral depress the heart muscle to such an extent that the slightest exertion may be fatal.

Chronic poisoning, *i.e.*, the chloral habit, is not uncom-

mon. In addition to the symptoms mentioned on page 130, the chloral habitué is subject to skin eruptions, due, it is thought at least in part, to changes in the circulation in the superficial blood-vessels as the result of their frequent dilation. The symptoms of defective metabolism are likely to be particularly marked, because chloral interferes with metabolic processes by its direct action on protoplasm, as well as through its influence on the nervous system. Therefore, if the habit is continued for a long time, fatty degeneration of the organs, such as occurs in chloroform poisoning, is likely to result.

The chloral habitué acquires a **tolerance** for the drug so that relatively large doses can be taken without causing acute poisoning.

When treating a patient for chronic poisoning the use of the chloral has to be stopped gradually, for, if it is suddenly withheld a condition similar to delirium tremens may occur. Otherwise, the treatment is about as described on page 131.

OTHER DRUGS BELONGING TO THE CHLORAL GROUP

The various drugs of this group have been prepared in the endeavor to secure a preparation that would have the hypnotic effects of chloral without its tendency to depress the heart muscle and to interfere with metabolism. The ones most commonly used are: Veronal and its sodium salt, medinal; paraldehyde; trional and sulphonal.

Veronal, known also as *barbital,* dose, 5–15 grs. (0.3–1.0 gm.)

Medinal (the sodium salt of veronal) 5–10 grs. (0.3–0.6 gm.)

Veronal is not very soluble in cold solvents and is, therefore, generally administered in hot milk or other hot drink. Medinal is more soluble than veronal and can be given hypodermically or by rectum, as well as by mouth. Suppositories can be had for rectal administration.

These drugs are thought to act solely upon the central nervous system, chiefly the psychic centers, and the condition they produce very closely resembles that of

natural sleep. They will, as a rule, if the patient is not in pain, induce unconsciousness in from 20 minutes to half an hour, but they do not depress the sensory centers sufficiently to act as analgesics. The patient on awakening is likely to be less depressed than after the use of most other narcotics.

If **poisonous doses** are taken the individual will gradually pass into a state of coma and death will occur from paralysis of the respiratory center. Death has been reported from a dose of 150 grains. The **treatment for poisoning** is the same as for that by chloral.

Paraldehyde, dose, 15–60 minims (1–4 c.c.) or, to overcome the excitement of delirium tremens, it is sometimes given by rectum in doses of from 2ʒ–½ oz. (8–15 c.c.)

Paraldehyde has a very unpleasant **flavor** and thus should be given in capsules or diluted with flavored syrup.

Paraldehyde irritates the **mucous membranes** and thus may cause a slight transitory reflex stimulation of the breathing and circulation. Also, partly because of this action but chiefly on account of its unpleasant taste, it may cause nausea and vomiting.

Otherwise, the **action** of paraldehyde is similar to that of veronal and it is even less likely to cause depression and poisoning, so that, when necessary, it can be used in comparatively large doses. For this reason it is very frequently used to overcome sleeplessness due to intense excitement. When large doses are needed they are generally given by rectum as, if given by mouth, they are likely to cause vomiting.

Trional, tetronal and **sulphonal** are all used in **doses** of 10–30 grs. (0.6–2.0 gm.)

These drugs, especially sulphonal, are not either readily absorbed or excreted. As they are more soluble in hot than in cold solvents they are given with hot drinks. They do not produce their effects quickly and thus trional and tetronal must be given about ½ to 1 hour, and sulphonal 2–3 hours before the time for sleep.

The action of these drugs after absorption is very similar to that of veronal, but, as they are slowly excreted, drowsiness and lack of energy are likely to be experienced the day following their use. For the same reason, their constant use is more likely, after a time, to promote the conditions mentioned on page 130.

Adaline (not official), dose 15 grains (1 gm.).

The action of adaline is similar to that of veronal, but weaker.

Acetal (not official), dose 1–2ʒ (4.0–8.0 gm.). The action of acetal resembles that of sulphonal.

Amylene hydrate (not official), dose 30–60 minims (2.0–4.0 c.c.). This resembles chloral in its action, but it is only about half as strong and it does not depress the heart muscle as much as chloral. Its narcotic action is quite frequently preceded by a stage of excitement.

Bromal hydrate (not official), dose 3–5 grs. (0.2–0.3 gm.).

This resembles chloral in its action, but it is more poisonous.

Bromoform (not official), 2–3 minims (0.13–0.2 c.c.).

This acts like chloral but it is more depressing and it has a greater tendency to interfere with metabolism. Also, it depresses the sensory areas of the cerebrum, and thus lessens pain. It is rarely used as a hypnotic, but is occasionally employed to overcome the spasmodic contractions of whooping cough.

Bromural (not official), dose 5–15 grs. (0.3–1.0 gm.).

This acts like veronal, but it is weaker.

Butyl chloral hydrate or croton chloral (not official), dose 5–20 grs. (0.3–1.3 gm.).

The action of this drug is practically the same as that of chloral hydrate, from which it is prepared. It was formerly thought to have a specific analgesic action on the nerves of the face and was therefore much used in the treatment of facial neuralgia, but experiments have shown that it has no such action.

Chloralamide or chloralformamide (not official), dose 15–30 grs. (1.0–2.0 gm.).

This acts like chloral, but it is less irritating to the stomach. Its narcotic action, however, is slower and less certain.

Chloral camphor is used externally as a counterirritant.

Chloralose (not official), dose 5–10 grs.

This acts like chloral but it does not depress the reflex centers nor, to the same extent that chloral does, the heart muscle. Large doses may be followed by muscular twitching and convulsions will occur in poisoning.

Chloretone, dose 10–15 grs. (0.6–1.0 gm.).

hen applied to abraided surfaces, as ulcers, or mucous membranes, chloretone depresses the sensory nerve-endings in the part and thus relieves pain and checks irritation. After absorption, it acts like chloral, but is rather weaker. It is sometimes used to check vomiting, which it does by lessening the sensitiveness of the stomach and by its sedative action on nerve-centers.

Dormiol or **amylene chloral** (not official), dose 20 m.–1 (1.3–4.0 c.c.).

The action of dormiol is the same as that of amylene hydrate.

Hedonal (not official), dose 30 grains (2 gm.).

This acts like veronal, but is not as reliable, for it often fails to produce hypnosis.

Hypnone (not official), dose 10–15 m. (0.6–1.0 c.c.).

This is a mild, but not very efficient, hypnotic.

Isopral (not official), dose 5–8 grains (0.3–0.5 gm.).

This acts like chlorotone.

Methylal (not official), dose 1–2ʒ (4.0–8.0 c.c.).

This acts like sulphonal.

Neuranol (not official), dose 5–30 grs. (0.3–2.0 gm.).

This acts like veronal.

Proponal (not official), dose 5–15 grs. (0.3–1.0 gm.).

This acts like veronal.

Urethan, dose 30 grs.–1ʒ (2.0–4.0 gm.).

This acts like veronal, but is less powerful and often fails to produce hypnosis. It is changed to urea in the system and thus acts as a diuretic.

THE BROMIDES

The bromides are salts of hydrobromic acid and one or other of the alkalies, such as potassium, sodium, ammonium. The alkali of a bromide is indicated by the name of the salt. **Hydrobromic acid** (HBr) is a combination of the elements hydrogen and bromine.

All the bromides have a salty, bitter taste.

Preparations and dosage:

Potassium bromide, 10–60 grs. (0.6–4.0 gm.).
Sodium bromide, 10–60 grs. (0.6–4.0 gm.).
Ammonium bromide, 10–30 grs. (0.6–2.0 gm.).
Lithium bromide, 10–30 grs. (0.6 2.0 gm.).
Calcium bromide, 30–60 grs. (2.0–4.0 gm.).
Strontium bromide, 30–60 grs. (2.0–4.0 gm.).
Hydrobromic acid (10% solution) 30 m.–2ʒ (2.0–8.0 c.c.).

New and Unofficial Preparations.—Bromipin or bromiol (*a compound of bromine and sesame oil*).

This is put up in different strength solutions and consequently the dosage varies considerably. It is best administered in a flavored syrup and shaken or beaten until the oil is emulsified. When given in this way it does not irritate the mucous membrane and, for this reason, it is sometimes substituted for an alkaline bromide when its use has to be continued for some time.

Brovalol (*a compound of bromine and valeric acid*) 5–10 grs. (0.3–0.6 gm.)

There are some bromide compounds mentioned with the chloral group for, because of their other constituents, they resemble the drugs of that series more than the inorganic bromides.

Administration.—The bromides should be well diluted.

Fate in the Body.—The bromides are absorbed rapidly through mucous membranes. They are eliminated chiefly through the kidneys, but traces may be found in the sweat, feces and, when the mammary glands are active, the milk. Elimination is slow, it is hastened by the administration of excess sodium chlorid and, on the other hand, it is

retarded by the withdrawal of sodium chlorid from the diet. The reason for this is that most of the tissues and the kidneys react to the bromides in the same manner that they do to sodium chloride, and, if there is less sodium chloride in the blood than usual, the kidneys do not remove the bromide, while if the quantity of sodium chloride is increased, excretion of salts, both chloride and bromide, is accelerated until the gross per centage of salts in the blood is normal.

The actions of the bromides before absorption are due to their salt characteristics described on page 47, and, after absorption to their bromine ion. Thus, with slight exceptions mentioned later, the actions of the different bromides are almost identical.

Actions:

Bromides do not affect the unbroken **skin** but, when they are applied to **surfaces denuded of skin or to mucous membranes,** they cause irritation and a slight depression of sensory nerve-endings in the area.

After absorption, the bromides, in therapeutic doses, have a slight, but prolonged, depressant action on **nerve-centers,** except those in the medulla. It is thought that they cause depression by some, as yet unknown, action upon the synapses of the neurones which interferes with the passage of impulses.

Very large doses may also depress medullary centers and, possibly, the muscle tissue of the heart and arteries.

The bromides have the usual action of diffusible salts upon the **excretion of urine.** This was discussed in the section on diuretics.

Effects of Actions:

If a concentrated solution of a bromide is applied to a **raw surface or mucous membrane** it will induce irritation which will be followed by a slight anesthesia.

When taken by mouth, the bromides increase the flow of saliva and, because of their salt action (described page 47) they tend to cause thirst. If concentrated enough to have a strong salt action, and thus promote

irritation, they are likely to cause nausea and vomiting, otherwise, by their action after absorption, they tend to check these conditions.

After the absorption of bromides, as the direct result of their action upon the cord and brain, the following effects occur.—1. Reflex response to stimulation is retarded and diminished; *e.g.*, irritation is not as likely to induce coughing, vomiting or convulsions. 2. Muscle tone is diminished. 3. Muscular coördination is interfered with. This, following small doses, is not always very obvious but, after large doses, it shows in awkwardness and uncertainty of movements. 3. The perception of sensations (sight, hearing, taste, touch, etc.) is less keen, but sensory centers are not sufficiently depressed, even by large doses of bromides to prevent the perception of pain if it is severe. 4. Psychic powers are diminished and a condition of drowsiness, apathy, and lassitude is promoted and, if conditions are favorable, a state resembling sleep will follow, but the bromides are not as likely to induce unconsciousness as most of the drugs of the chloral group. Even when sleep does occur, the individual upon awakening is likely to be still mentally and physically depressed, because the drug is so slowly eliminated.

As the result of lessened muscle tone catabolism is below par and thus the temperature is likely to be somewhat reduced.

As the result of general depression breathing is slowed and the heart action is slowed and somewhat weakened.

Sexual instinct is lessened. It is not known if this is due to the general depression or to direct action upon special nerve centers.

The excretion of urine is slightly increased.

After even a few doses of bromide, various forms of eruptions may appear on the **skin**, especially on the face and neck. The reason for this is not known; formerly, it was attributed to irritation during excretion, by the sweat glands but, it is now considered, the quantity excreted in this way is not large enough to induce such irritation.

Nevertheless, frequent bathing of the threatened parts tends to prevent the condition and when, as in the treatment of nervous conditions, such as epilepsy and chorea, it is desired to continue the use of a bromide for some time, it is most important to prevent such eruptions for they may be very annoying to the patient.

Differences in Action.—The bromides, sodium, potassium and ammonium, are generally considered more efficacious than the lithium, strontium and calcium salts. The potassium ion of potassium bromide tends to have a slight depressant effect upon heart muscle. The ammonia of ammonium bromide is said to induce a slight reflex stimulation of the heart action and breathing. The lithium may possibly increase the excretion of urine more than the other salts.

Common therapeutic uses of the bromides are: To lessen reflex response to irritation, as coughing, vomiting, convulsions.

To check excessive nervous irritability, as in exophthalmic goiter and chorea, and extreme excitement, as in delirium tremens.

To inhibit convulsions such as occur in strychnine poisoning, tetanus and epilepsy.

To lessen sexual excitement such as sometimes occurs in the insane and as the result of irritation of the external sex organs by disease or following operations upon these parts.

To lessen pain that is due to hypersensitiveness, as in neurasthenia.

Toxicology.—As the excretion of bromides is slow, they are likely to cause cumulative poisoning, known as **bromism,** if they are taken for any length of time.

The symptoms are: Apathy and drowsiness; the patient is depressed and melancholy; unable to remember readily, even for a short time, or to do mental work; muscular coördination is so defective that movements are uncertain and the individual is likely to stagger when walking; reflex response is diminished and thus irritation will not

induce the usual degree of muscular contraction or secretion. The depressed condition of the nervous system gradually interferes with the functioning of the other organs and the abnormal conditions described on page 130, appear. Also there will be an eruption usually of the acne type, which may be confined to the face and neck, but, especially if the use of the drug is not discontinued, is likely to become scattered over the body.

The treatment consists in stopping the use of the drug, and giving all the sodium chloride and water possible, so as to hasten its elimination. Strychnine and caffeine are likely to be prescribed, if the bromic has not been used to check convulsions, as in the treatment of epilepsy.

The symptoms of acute poisoning are.—Profound apathy even stupor. Slow, shallow breathing and slow weak pulse; the condition may persist for some time, but the drug is not very toxic and thus death has seldom, if ever, occurred.

The treatment for acute poisoning is the same as for bromism.

THE OPIUM SERIES OF NARCOTICS AND ANALGESICS

OPIUM AND ITS ALKALOIDS

Opium is derived from the dried juice of the *Papaver somniferum*, a species of poppy which grows principally in Asia Minor, Turkey, Persia, China and India. It contains a number of alkaloids the more important of which are: Morphine, codeine, papaverine, narcotine and thebaine. Of these only the four first mentioned are extracted for medicinal use. Opium also contains several acids, but these have no important action, and gums and other inert substance.

Preparations and dosage of opium and its alkaloids:

Opium.—Powdered opium, ¼–2 grs. (0.015–0.13 gm.) contains 12% morphine.

Deodorized opium, ¼–2 grs. (0.015–0.13 gm.) *The substances which give opium its disagreeable odor and the*

narcotine have been removed, otherwise this is the same as powdered opium.

Extract of opium, ⅛–1 gr. (0.008–0.06 gm.) contains 20% morphine.

Pills of opium, each pill contains 1 gr. (0.06 gm.) of powdered opium.

Dover's powder, 5–10 grs. (0.3–0.6 gm.) each 10 grs. powder contains 1 gr. of opium, 1 gr. ipecac, and 5 grs. of sugar of milk.

Tincture of opium (laudanum), 3–15 m. (0.2–1.0 c.c.) contains 10% opium).

Deodorized tincture of opium, 3–15 m. (0.2–1.0 c.c.).

Camphorated tincture of opium (paregoric), 1–4ʒ (4.0–16.0 c.c.).

Each dram contains ¼ gr. of opium (which is equivalent to 132 gr. of morphine) oil of anise, camphor, benzoic acid and glycerine.

Tincture of ipecac and opium, 5–15 m. (0.3, 1.0 c.c.) contains 10% opium.

Opium vinegar (Black drop) 3–15 m. (0.2–1.0 c.c.). This is opium extract dissolved in dilute acetic acid.

Wine of opium 3–15 m. (0.2–1.0 c.c.).

Compound tincture of opium (Squibb's diarrhea mixture) 1ʒ (4.0 c.c.).

Mistura glycyrrhizæ composita (Brown's cough mixture) 30 m–1ʒ (2.0–4.0 c.c.). *Contains 12 parts paregoric.*

Pantopon ¼–½ gr. (0.015–0.03 gm.). A non-official preparation of the alkaloids of opium.

Pleistopon ¼–½ gr. (0.015–0.03 gm.). Similar to pantopon, but minus narcotine.

Morphine preparations:

Morphine ⅛–½ gr. (0.008–0.03 gm.).

Morphine sulphate, same as morphine.

Morphine hydrochloride, same as morphine.

Morphine meconate, same as morphine.

Majendie's solution (not official) 5–10 m. (0.3–0.6 c.c.). *Each ounce contains 16 grs. of morphine. This preparation is sometimes used for hypodermic administration. It must*

be kept in dark colored bottles and an old solution should not be used, for the preparation soon loses its strength and the morphine may be changed to apomorphine. Solutions that have undergone change are usually of a brownish color and sometimes contain a fungus.

Apomorphine hydrochloride (*an artificial alkaloid prepared from morphine*). Emetic dose, 1/10 gr. (0.006 gm.).

Expectorant dose, 1/30 gr. (0.002 gm.).

Analgesic dose, 1/20 gr. (0.003 gm.).

Narcophine (non-official) 1/4–1/2 gr. (0.015–0.03 gm.). *This consists of 33 per cent. morphine meconate and 67 per cent. narcotine meconate.*

Heroine hydrochloride (*an artificial alkaloid of morphine*) 1/24–1/6 gr. (0.0025–0.01 gm.).

Heroine hydrobromate, same as above.

Peronine or benzyl morphine (*an artificial alkaloid of morphine*) 1/4–1 gr. (0.015, 0.06 gm.).

Dionine or ethyl-morphine, same dosage as peronine and it is also used in the eyes in, usually, a 5 per cent. solution.

Codeine preparations:

Codeine 1/4–1 gr. (0.015–0.06 gm.).

Codeine sulphate, same as codeine.

Codeine phosphate, same as codeine.

Eucodeine (methyl-codeine-bromide) 1/2–1 gr. (0.03–0.06 gm.).

Apocodeine hydrochloride (a non-official alkaloid prepared from codeine) 1/2–1 gr. (0.03–0.06 gm.).

Papaverine preparations:

Papaverine hydrochloride 1/2–2 grs. (0.03–0.12 gm.). For local use 2–4 per cent. solutions are employed.

Papaverine sulphate, same as above.

A tolerance for opium and its alkaloids is readily established so that the habitué can take amounts which would be highly poisonous to people not addicted to their use.

On the other hand, some people, especially the old and the very young, are exceedingly **susceptible** to the influence of opium and its alkaloids. For this reason, the **dosage**

for children is always somewhat smaller than the amount computed by the rules given in the section on Dosage.

OPIUM AND MORPHINE

Fate in the Body.—Morphine is readily absorbed through mucous membranes and from subcutaneous tissues. The effects of a dose being observed in from 2–5 minutes. Opium is not absorbed as quickly as morphine because its gums and some of the other inert constituents retard its absorption. Neither of the drugs is absorbed through the unbroken skin. After absorption, a small amount of a dose is oxidized, the remainder is excreted fairly rapidly. A small amount passes through the kidneys and traces are sometimes found in the saliva, sweat and milk, but the greater part of a dose is eliminated through the stomach and intestine. After being excreted into the latter organs, there is some reabsorption of the drug and the processes of absorption and excretion will continue until all the drug is destroyed or eliminated.

Actions.—The actions of morphine and opium are similar, those of opium being mainly due to its morphine. Were it not that narcotine intensifies the action of morphine on nerve-centers, opium would be less depressant than the latter but, because of its narcotine, it is, if anything, more narcotic. Opium, because of some of its minor alkaloids, also depresses intestinal action more than morphine. Otherwise, the following description of morphine actions can be applied to opium.

Morphine has no action upon the **unbroken skin.** When applied to **mucous membranes and wounds** it will check pain in the part, but, it is thought, this is almost, if not entirely, due to the action of the drug upon the nerve-centers after it has been absorbed.

Actions after absorption:

On the Cerebrum.—Morphine depresses the sensory centers, especially those in which impulses which give rise to a sensation of pain are transmitted to the centers of consciousness. Also, it depresses the psychic areas to

a slight degree. Moderate doses have little or no direct effect upon the motor areas, large doses may cause slight depression.

On the Cerebellum.—Large doses cause slight depression.

On the Medulla.—Morphine **depresses**: The respiratory center; the secretory centers, except the sweat center; and the cough center. Following moderate doses, the vagus, vasoconstrictor, sweat, and pupil-contracting centers are **stimulated**, but some authorities consider that this stimulation is due to the partial asphyxia promoted by the depression of the respiratory center.[1] Occasionally the vomiting center is stimulated, but, it is thought, this is done by substances, probably apomorphine, into which the morphine is changed in the tissues.

On the Spinal Cord.—Morphine lessens the sensitiveness of the reflex centers.

On the Intestine.—It is thought that morphine depresses ganglia on motor neurones situated in the intestinal wall.

Of the above actions, the most important ones are: The depression of the sensory and respiratory centers and of the intestinal ganglia and, as a means of observing overdosing, the stimulation of the pupil contracting center.

Effects of Actions.—Pain that is continuous is overcome, but any new, sharp sensation will be felt temporarily. All the senses (*e.g.*, sight, hearing, touch) are rendered less acute and the pathway of impulses to the psychic centers is more or less blocked. If the blocking is extreme, a state of unconsciousness resembling sleep occurs, if not, the condition induced will be simply one of quiet and drowsiness such as one may experience when reclining at rest in a quiet and dimly lighted place.

The psychic powers of concentration, reasoning, judgment, will, are reduced, but, unless profound narcosis is produced, the depression of the psychic centers, is not, as a rule, sufficient to interfere with the conditions of their protoplasm that constitute memories and are thus the

[1] The nature and results of asphyxia are described on page 96.

basis of imagination; this faculty consisting in using the impressions (memories) that have been made in the cerebrum to form the pictures or thoughts that we call ideas and dreams and, as previously stated, depression of the intellectual capacities which require mental concentration for their exercise allows the imagination to become unusually active. This effect of morphine is more pronounced in some individuals than others. A person who is thus influenced may be so entertained with his imaginations that he becomes oblivious of his surroundings and is able to forget worries, annoyances and disappointments; even when sleep is not induced. Some authors are said to have conceived the plots of their novels and scientists the ideas which led to inventions or important discoveries while under the influence of morphine, but it is improbable that the ideas conceived were utilized until the effects of the drug had subsided because, until they did, the energy and the powers of application, concentration and judgment, necessary for such work, must have been lacking.

The quiet and lethargy induced promote muscular relaxation, but single therapeutic doses of morphine do not depress the motor areas of the cerebrum or the reflex centers of the brain and cord sufficiently to cause much reduction of muscle tone and even poisonous doses do not cause as much muscular depression as chloral and the bromides. Thus, though morphine will lessen and retard response to some reflexes, as, for examples, coughing and vomiting that is due to irritation, it will not check convulsions. The continuous use of morphine, however, will result in a gradual loss of tone.

Large doses of morphine will, because of their action on the cerebellum and cerebral motor areas, interfere with proper muscular coördination, so that the individual may stagger when walking.

Morphine tends to make the breathing slow and shallow and death from morphine poisoning is almost invariably due to paralysis of the respiratory center. Therefore the

rate of the breathing is the most important thing to observe when watching for symptoms of overdosing.

The blood-vessels of the skin are dilated and thus the skin is flushed, but, after moderate doses of morphine, the other vessels, except those of the brain, heart and lungs,[1] are contracted. This tends to make the **heart action** slow and stronger, and the former effect (slowing) is accentuated by the stimulation of the vagus. Even after poisonous doses, when artificial respiration is necessary, the pulse may remain fairly strong.

After moderate doses of morphine, the **pupils** become somewhat contracted and, after poisonous doses, the contraction becomes so extreme that the term *pin-point pupils* has been applied to the condition.

The secretion of sweat is slightly increased, but all other **secretions** are checked.

The lessened secretion of intestinal mucus and the diminished peristalsis, (resulting from the depression of the motor ganglia in the **intestinal wall**) cause constipation. This effect is induced to a greater degree by opium than morphine.

The bodily inactivity and consequent muscular relaxation abate **metabolism** and so lessen heat production; the increased amount of blood at the surface of the body and the excess perspiration favor loss of heat, thus the **temperature** is lowered.

The reduction of the body's supply of oxygen (due to the effect on breathing) interferes with oxidation and causes an increase of lactic acid and glucose in the blood and urine. Nevertheless, for some unknown reason, in diabetes, morphine tends to lessen the amount of glucose in the urine.

The various effects of morphine on the body promote a general physical and mental depression of which the individual becomes acutely aware as soon as the effect of the drug on the sensory centers has subsided.

[1] These vessels, it will be remembered, are not controlled by the vasoconstrictor center.

To Summarize the Usual Results of Therapeutic Doses of Morphine.—A state of drowsiness and lethargy is promoted in which the higher intellectual capacities are depressed, but the imagination is unusually active, even, as a rule, when so-called sleep occurs. Pain and anxiety are relieved. The breathing is considerably slower and more shallow than in normal sleep, also, the pulse is slower, though it is strong. The skin, especially that of the face, is slightly flushed and somewhat moist, but mucous membranes are dry. The pupils are contracted.

After the primary effects of the drug subside, the patient is depressed, exceedingly thirsty, and may be nauseated and have a headache.

Due to some unknown idiosyncrasies, some of the following untoward effects occasionally follow the use of morphine: The conditions of acute poisoning are caused by ordinary therapeutic doses. Heart block, described page 54. Nausea and vomiting. Pronounced constipation or diarrhea. Fever. Rash. Diminished secretion of urine, this is particularly likely to occur, as well as other bad effects when the individual has nephritis.

Common therapeutic uses of opium and morphine are:

To relieve pain.

To check intestinal peristalsis in such conditions as peritonitis, intestinal hemorrhage, severe diarrhea, and following operations on the bowel. Opium is most commonly used for this purpose.

To check severe vomiting and cough.

To cause diaphoresis, Dover's powder is used.

To lessen worry and quiet the heart action in such conditions as hemorrhage, asthma and angina pectoris.

As a preliminary to general anesthesia.

Toxicology.—The **symptoms of acute poisoning** are manifested in three degrees. If the dose taken is not excessive only the conditions of the first or second degree will be induced, but after a very large dose, unless antidotal measures are successful, the patient will pass through the two first stages to the third quite rapidly.

The symptoms of the first degree consist simply in the accentuation of the ordinary effects of the drug, thus: The breathing becomes slower and more shallow; the pupils more contracted; the face very flushed; perspiration profuse; the pulse slower, but it usually remains strong. The patient is in a state of lethargy, but can be quite easily aroused and will answer questions sensibly. Sometimes there is nausea and vomiting.

In the second degree of poisoning these symptoms are still more pronounced. The breathing may become as slow as 5 or 8 movements per minute, or there may be Cheyne-Stokes breathing, and there is cyanosis. The pupils are so contracted that the condition is known as *pin-point pupils*. The patient is in a state of stupor, but can still be aroused, though he can only be kept awake with difficulty. Perspiration is profuse. The pulse, as a rule, is still slow and strong.

The third stage is that of narcosis or coma. The patient cannot be aroused. The breathing movements are irregular, and reduced to 3 or 4 per minute and tend to cease, thus artificial respiration is necessary to maintain life. Cyanosis is extreme. The pulse gradually becomes weak and, unless treatment is successful, the pupils dilate widely and collapse occurs.

There are certain **differences between the conditions in morphine poisoning** and other depressant drugs which make it necessary to modify the treatment for morphine poisoning. These are: (1) The heart action is not weakened in the early stages and, therefore, as it is most important to keep the patient awake and breathing, the patient is not kept quiet. (2) As the result of the action of the drug on the sensory centers, any one form of stimulus ceases to be perceived after a short time and thus, when the patient fails to respond to a stimulus, another should be tried. (3) As the drug passes back and forth between the stomach and intestines and the blood, periodic lavage of the stomach and intestines is indicated.

The treatment for acute poisoning consists in giving: (1)

An emetic and gastric lavage. The latter is repeated at intervals of from ½ to 1 hour. Sometimes potassium permanganate is prescribed for the lavage, in order to oxidize the morphine; but many investigators have not found that it does this and consider that it is injurious to the gastric mucous membrane. (2) Colon irrigation, which is repeated at intervals of about 4 hours. (3) Hot coffee, by mouth, if possible, if not by rectum. (4) Caffeine and atropine by hypodermic.

The patient should be kept in a cool, well aired, light room and, if possible, walking about. If the poisoning is so advanced that walking is impossible, artificial respiration will probably be necessary and various forms of stimula are used, *e.g.*, the rectum is stretched; vigorous percussion is applied; large applications of mustard paste are made to the skin; the faradic current is sometimes used. Formerly cold douches were given, but they are rarely used now, because chilling the patient increases the danger of pneumonia, a not uncommon sequence of morphine poisoning when artificial respiration is necessary.

The symptoms of chronic poisoning in the early stages vary according to the amount of drug that the individual uses. Many habitués, for a time, only take large enough doses to stimulate their imagination and give them the characteristic sensation of well-being. In such case, the bad results of the drug's action may be slow in appearing, but morphine cannot be used, even in small doses, for any length of time without the onset of physical and mental deterioration and thus, sooner or later, the symptoms described on page 130 appear. Also, the pupils of the eyes remain more contracted than usual and the individual is likely to perspire profusely and to suffer from intestinal cramps—due largely to the accumulation of gas, as the result of the constipation. When not under the influence of the drug, the habitué is likely to be exceedingly depressed and melancholy, nervous and irritable, unable to concentrate the attention either upon work or pleasure, and the craving for the drug becomes so great that he will

lie and steal to get it. As the habitué usually takes the drug by hypodermic his skin is likely to show marks of the needle and he frequently has hypodermic abscesses, for he becomes careless and slovenly as his mental capacities diminish and ceases to be even cleanly, much less to take aseptic precautions.

There are several special **treatments for chronic morphine poisoning.** Whatever the special points, those mentioned on page 131 are considered of importance. As a rule the drug is either withdrawn gradually, smaller doses being given each day, or another drug with somewhat similar action, as codeine or hyoscine, is substituted for a time; because sudden cessation of the morphine effects causes the patient to suffer intensely from physical and psychic depression. In all treatments cathartics are used freely in order to hasten the elimination of the drug.

NARCOPHINE AND ARTIFICIAL ALKALOIDS OF MORPHINE

Narcophine is said to depress the respiratory center less than morphine and to have greater analgesic power. The latter effect is due to the narcotine which, as previously stated, intensifies the action of morphine on the sensory centers.

Heroine acts like morphine but it does not relieve pain nor induce sleep as readily and it is more depressing to the respiratory center and, therefore, more likely to cause poisoning.

It induces **"habit"** and the habitués take it by mouth, hypodermically and by snuffing. When it is used as snuff, it produces atrophy of the nasal membrane.

The common **therapeutic use** of heroine is to relieve cough. **Dionine** and **peronine** act like codeine. Dionine also, when applied to the eye, acts as a local anesthetic and it dilates the pupil.

Apomorphine in small doses may have a mild morphine action, but it stimulates the vomiting center and the conditions thereby produced overcome the sedative action

on the cerebrum. Even in doses too small to induce emesis it has a nauseant action and, as the result of this, increases and fluidifies the bronchial mucus, therefore, it acts as an expectorant. When used as an emetic it is given by hypodermic and will almost invariably produce profuse emesis in a few minutes.

CODEINE

Codeine, as previously stated, is one of the alkaloids of opium.

Codeine acts like morphine but it is only about one-fourth as powerful a drug and, even in relatively large doses has the following differences:

Codeine does not depress the respiratory center to the same extent as morphine, nor is it as likely to induce constipation, not to overcome severe pain. Neither does it stimulate the imagination in the same way as morphine and its use is not followed by as great depressing and therefore, it does not induce the craving which is probably largely responsible for habit. Doses even moderately larger than those commonly used in therapeutics will stimulate the spinal cord and cause restlessness and, sometimes, twitching of the muscles.

Codeine is used chiefly to check cough and to overcome mild pain.

APOCODEINE

Apocodeine is prepared from codeine in the same manner as apomorphine is from morphine, but its action is not at all the same as either apomorphine or codeine. It is described with the depressants of sympathetic nerve-endings.

PAPAVERINE

Papaverine, as previously stated, is an alkaloid of opium.

When applied to mucous membrane or injected under the skin, papaverine causes a local mild irritation that is followed by a moderate degree of analgesia.

After absorption, papaverine acts upon **nerve-centers** in about the same manner as morphine, but it is only about one-half as powerful and, even in relatively large doses, it does not depress the respiratory center to a great degree. Papaverine also has a direct depressant effect upon *cardiac tissue* and upon the **plain muscle tissue** of the bronchial tubes, arteries, stomach, intestines, gall-bladder, bile passages, urinary ducts.

As the result of its action on plain muscle tissue papaverine tends to overcome spasmodic contractions such as occur in asthma, angina pectoris, intestinal and renal colic and **it is used chiefly** for such purposes and to check cough and vomiting, which it does, like morphine and codeine, by its central action.

CANNABIS INDICA

Cannabis Indica (Indian hemp) **is obtained** from hemp grown in the East Indies and other warm climates. Various preparations of the drug, hashish, bhang, etc. are much used in the Orient because of their pleasurable effects, which resemble those of morphine.

Preparations and dosage:

Extract of cannabis indica ¼–1 gr. (0.015–0.06 gm.).

Fluidextract of cannabis indica 1–5 m. (0.06, 0.3 c.c.).

Tincture of cannabis indica, 10–30 m. (0.6–2.0 c.c.).

Cannabis indica tends to have the same depressant **action** upon **nerve-centers** as morphine and, like morphine, it will relieve pain, but it does not produce sleep as readily; it causes less subsequent depression; and it is not as likely to cause nausea and vomiting. Unfortunately, the drug deteriorates rapidly and thus, in countries at a distance from its origin, its action is not reliable.

LUPULIN OR HUMULUS

Lupulin or humulus **is prepared** from hops. It has a mild sedative **action** on nerve-centers.

Fluidextract of lupulin (unofficial) 3 m. (0.2 c.c.).

LACTUCARIUM

Lactucarium is obtained from the Lactura virosa or garden lettuce.

Dosage:

Syrup of Lactucarium 1–2 ʒ (4.0–8.0 c.c.).

Tincture of Lactucarium 10–30 m. (0.6–2 c.c.).

Lactucarium has a mild sedative action upon nerve-centers.

It is used chiefly for children, as a substitute for morphine, to relieve pain, and the syrup is used to relieve cough.

ANALGESIC ANTIPYRETICS

The drugs classed under this heading are prepared from coal tar or coal tar derivatives. The principal ones are acetanilid or antifebrine, antipyrine, and acetphenetidin or phenacetine.

Preparations and dosage:

Acetanilid, 2–10 grs. (0.13–0.6 gm.).

Antipyrine, 5–20 grs. (0.3–1.3 gm.).

Antipyrine salicylate, 5–20 grs. (0.3–1.3 gm.).

Phenacetine, 5–15 grs. (0.3–1.0 gm.).

Non-official, preparations that resemble acetanilid.

Antikamnia, 5–15 grs. (0.6–1.0 gm.).

Antinervine, 5–15 grs. (0.6–1.0 gm.). This consists of acetanilid, ammonium bromide, and salicylic acid.

Exalgine, 2–10 grs. (0.13–0.6 gm.).

Thalline, 5–10 grs. (0.3–0.6 gm.).

Non-official preparations that resemble antipyrine:

Migrainin, 5–15 grs. (0.3–1.0 gm.). This consists of antipyrine, caffeine and citric acid.

Pyramidon, 1–5 grs. (0.06–0.3 gms.).

Pyramidon camphorate, 5–15 grs. (0.3–1.0 gm.).

Tussol, 1–5 grs. (0.6–0.3 gm.).

Non-official preparations that resemble phenacetine.

Analgen, 3–10 grs. (0.2–0.6 gm.).

Asaprol, 5–30 grs. (0.3–2.0 gm.).

Benzanilide, 3–10 grs. (0.2, 0.6 gm.).

Exodyne, 3–10 grs. (0.2, 0.6 gm.).

Hydracetine, 3–10 grs. (0.2, 0.6 gm.).

Iodophenine, 3–10 grs. (0.2, 0.6 gm.).
Methacetine, 3–10 grs. (0.2, 0.6 gm.).
Phenocoll hydrochloride, 5–20 grs. (0.3–1.3 gm.).
Phenocoll salicylate, 10–30 grs. (0.6–2.0 gm.).
Phenolid, 3–10 grs. (0.2–0.6 gm.).
Thermodine or phenacetine urethan, 5–15 grs. (0.3–1.0 gm.).
Triphenin, 5–15 grs. (0.3–1.0 gm.).
Thymacetine, 5–10 grs. (0.3–0.6 gm.).

There are also a number of compounds and derivatives of salicylic acid, which have both analgesic and antipyretic properties that are given under salicylic acid.

Administration.—Antipyrine should not be given at the same time as calomel for the two drugs combine and form a poisonous compound.

Sodium bicarbonate is sometimes prescribed with the drugs of this group, because it is thought to inhibit their tendency to depress the heart muscle. Formerly caffeine was much used for the purpose but it has been found to further, rather than prevent, bad effects.

Fate in the Body.—The analgesic antipyretics are readily absorbed from mucous membranes, their effects being observed in about 20 to 30 minutes. They are decomposed to simpler substances in the body and these are slowly eliminated, chiefly in the urine.

Actions:

These drugs have a mild depressant action upon the protoplasm of **bacteria.**

When applied to mucous membranes and raw surfaces, antipyrine stimulates vasoconstrictor nerve-endings and, after a transitory stimulation, depresses sensory nerve-endings slightly. **Acetanilid** is irritant to mucous membranes and raw surfaces and **phenacetine** has practically no effect upon them.

After absorption these drugs, with the exceptions mentioned, have, apparently, the same actions but these are not as well understood. It is thought, however, that the drugs: (1) Depress the portions of the thalami (masses

of gray matter in the under surface of the cerebrum) in which impulses which give rise to a sensation of pain are transmitted to the sensory areas of the cerebrum. (2) Either stimulate the heat regulating centers (which also are in the thalami and in the corpora striata) or else protect them from the action of toxins, which, it is believed, depress the centers so that they do not respond as readily as usual to increase in the temperature of the blood, as described on page 51. (3) Depress the centers of the cerebrum controlling consciousness to a slight degree and acetanilid also depresses the motor areas slightly. (4) First, stimulate the heart muscle very slightly and later depress it to some extent, acetanilid is particularly likely to do this. (5) Their decomposition products tend to unite with the hemoglobin of the red cells of the blood forming methemoglobin, and large doses destroy the red cells. The derivatives of the antipyrine members of the group are not as likely to do this as those of the other drugs.

Effects of Actions.—These drugs are all slightly antiseptic.

Antipyrine, when applied to **mucous membranes and raw surfaces,** causes contraction of the blood-vessels and consequent shrinking and drying of the tissues in the part, and it may check capillary hemorrhage, also, it acts as an anodyne. **Acetanilid** irritates such tissues and will increase the amount of blood in the area of its application, as described on page 49.

After absorption, all the drugs of this series have a slight analgesic effect and may overcome pain that is not severe, especially headache, neuralgia and neuritis. Also, they tend to lessen nervous irritability and, by so doing, if taken at bed-time, they favor the onset of sleep, but they are not hypnotic and, if taken when an individual is busy, they will not interfere even with intellectual work.

Phenacetine has the most pronounced sensory sedative effect and antipyrine the least, but antipyrine, by depressing **motor centers,** tends to lessen spasmodic contractions

such as occur in whooping cough and chorea. Poisonous doses of any of these drugs may cause muscular twitching or even convulsions, but the stimulation of the motor centers, which is responsible for the muscular contractions, is thought to be due to asphyxia (induced by the changes in the blood and its circulation) and not to the direct action of the drugs.

The **temperature** is reduced when it is abnormally high, but it is not affected, except by very large doses, when it is normal. The fall of temperature is brought about by increased loss of heat from the body, as the result of an increased amount of blood in the skin and increased perspiration; and the centers which produce these effects are stimulated by impulses going to them from the heat regulating centers.

The **pulse** is slightly accelerated for a short time but, after large doses and, in some individuals, even after moderate doses, it becomes slower and weaker.

The changes in the **blood** are not evident from therapeutic doses, except when the drugs are taken constantly, but methemoglobin does not combine readily with oxygen and thus, if it is formed, cyanosis and dyspnea will follow.

Untoward effects, due to some unknown idiosyncrasy, sometimes follow the use of even therapeutic doses of these drugs. Common ones are: Weak, slow pulse and faintness; nausea and vomiting. A skin rash, this is especially common after antipyrine. Excessive perspiration; cyanosis and dyspnea, these are not as likely to be caused by antipyrine as by acetanilid and phenacetine.

Therapeutic Uses.—Antipyrine is used locally to check capillary hemorrhage and, in a spray, in solutions of about 15 per cent., to lessen pain and congestion in the throat. It is used internally to check spasmodic contractions.

All the drugs of this series are used to lessen mild pain and nervousness and, occasionally, to lower the temperature in fever.

Toxicology:

Symptoms of Acute Poisoning are.—Burning sensation and congestion of the alimentary canal, this is especially

severe in acetanilid poisoning, nausea and vomiting. Cyanosis and dyspnea, these are less marked in poisoning by antipyrine and its compounds than the other drugs of the group. Slow weak pulse. Subnormal temperature and, sometimes shivering. There may be muscular twitching and even convulsions. Stupor and collapse.

The treatment consists in giving lavage; keeping the patient quiet and warm; supplying fresh air and, if possible, oxygen; giving demulcent drinks, as white of egg, milk and bland oils. Atropine is sometimes prescribed.

Chronic poisoning is quite common because many people, especially those who are nervous or subject to headaches form the habit of taking them. The symptoms are: Digestive disturbances; anemia; proneness to cyanosis and dyspnea on exertion; irritability; headache; and insomnia. The habit is not nearly as difficult to break as the morphine, alcohol and cocaine habits and the abnormal conditions and craving soon disappear when the drugs are withheld.

DRUGS WHICH PRODUCE THEIR CHIEF THERAPEUTIC EFFECTS BY THEIR ACTIONS ON PERIPHERAL NERVE-ENDINGS

Drugs which obtain their chief therapeutic effects by their actions on peripheral nerve-endings (known also as end-organs) are, like those which act upon nerve-centers, classified in two sub-groups, viz., stimulants and depressants.

Stimulation and depression of nerve-endings will have the same effects upon the organs with which they are connected as the stimulation and depression of nerve-centers. Thus, if a group of motor end-organs are stimulated, the contraction of the muscle in the part they supply will be more pronounced while, if the end-organs are depressed, the contraction will be lessened. If secretory end-organs are stimulated, the activity of the glands they supply will be increased and more secretion will be manufactured, but, if the end-organs are depressed, secretion will be lessened. If the inhibitory end-organs in muscle tissue are stimulated, contraction will be lessened, and, if those in a gland are stimulated, secretion will be inhibited; but, if the inhibitory end-organs are depressed, the activity of the parts they supply will be increased, because the motor or secretory impulses will have freer control of the part since there will be fewer or no inhibitory impulses discharged into it. If the receptors of the afferent fibers forming part of a reflex arc are stimulated, the activity of the muscle or gland in which the efferent fibers of the arc terminate will be increased, while, if the receptors are depressed, the activity of the organs will be lessened. If the receptors of a sense organ are stimulated, the sensation which the organ controls will be more acute,

but if the sensory receptors are depressed, the sensation they control, whether it be sight, smell, taste, pain, heat, cold, etc., will be diminished or lost, according to the degree of depression.

The manner in which drugs help or interfere with the functioning of the end-organs is unknown.

Some drugs only affect end-organs at their junction with muscle and these are said to act upon the myo[1]-neural[2] junctions or neuro-muscular junctions.

END-ORGAN DEPRESSANTS

The principal drugs belonging to this series are: The belladonna group and some local anesthetics and anodynes. Less important ones are: Agaricin, conium, gelsemium, spartein, nicotine, lobelia.

THE BELLADONNA SERIES

This group of drugs includes belladonna (deadly nightshade) stramonium (thornapple) hyoscyamus (henbane) and scopola.

The various plants from which these drugs are derived belong to the same botanical family as the potato and the egg plant.

The active principles of these drugs are the alkaloids atropine, hyoscyamine and hyoscine or scopolamine.

Preparations and Dosage of Belladonna Preparations.
Prepared from belladonna leaves:

Extract of belladonna, grain $\frac{1}{12}$–$\frac{1}{2}$ (0.005–0.03).

Tincture of belladonna, minims 5–15 (0.3–1.0 c.c.).

Rhinitis tablets, (unofficial) contain belladonna grain $\frac{1}{8}$, camphor grain $\frac{1}{4}$, quinine bisulphate grain $\frac{1}{2}$.

Belladonna ointment (this contains about 10 per cent. belladonna extract).

Belladonna plaster.

[1] From the Greek, *myos* = a muscle.
[2] From the Greek *neuron* = a nerve.

Prepared from the belladonna root:

Fluidextract of belladonna, minims 1–2 (0.06–0.12 c.c.).

Belladonna liniment.

Atropine Preparations:

Atropine, grain $\frac{1}{160}$–$\frac{1}{60}$ (0.0004–0.001 gm.).

Atropine sulphate, grain $\frac{1}{160}$–$\frac{1}{100}$ (0.0004–0.001 gm.).

Atropine oleate, for external use.

Atropine ointment.

Homatropine (an artificial alkaloid of atropine) grain $\frac{1}{100}$–$\frac{1}{60}$ (0.0006–0.001 gm.).

Methylatropine or Eumydrine (unofficial) grain, $\frac{1}{60}$–$\frac{1}{20}$ (1–3 mg.).

Stramonium preparations:

Extract of stramonium, grain $\frac{1}{4}$–$\frac{1}{2}$ (0.015–0.03 gm.).

Fluidextract of stramonium, minims, 1–2 (0.06–1.12 c.c.).

Tincture of stramonium, minims, 5–15 (0.3–1.0 c.c.).

Stramonium ointment.

Hyoscyamus preparations:

Extract of hyoscyamus, grains $\frac{1}{2}$–3 (0.03–0.2 gm.).

Fluidextract of hyoscyamus, minims 5–15 (0.3–1.0 c.c.).

Tincture of hyoscyamus, minims 15–ʒ1 (1.0–4.0 c.c.).

Hyoscyamine preparations:

Hyoscyamine sulphate, grain $\frac{1}{120}$–$\frac{1}{60}$ (0.0005–0.001 gm.).

Hyoscyamine hydrobromide, grain $\frac{1}{120}$–$\frac{1}{60}$ (0.0005–0.00 gm.).

Hyoscine preparation:

Hyoscine (scopolamine) hydrobromide, grain $\frac{1}{200}$–$\frac{1}{100}$ (0.0003–0.0006 gm.).

Scopola:

Extract of scopola, grain $\frac{1}{4}$–$\frac{1}{2}$ (0.015–0.03 gm.).

Fluidextract of scopola, minims 1–2 (0.06–0.12 c.c.).

The alkaloids and, consequently, the crude drugs of this group all resemble each other in their action; there are, however, a few points of difference and, therefore, the action of atropine will be described first and then the dissimilarities in the actions of the other drugs.

ATROPINE

Fate in the Body.—Atropine is readily absorbed through mucous membranes and from subcutaneous tissues, the effects of a dose being evident in from about ten to thirty minutes. Also, when it is in a fatty or alcoholic medium, atropine is slightly absorbed through the skin. Part of a dose may be oxidized in the body. The remainder is eliminated, mainly through the kidneys, but a small amount may be excreted in the milk when the mammary glands are active.

Actions.—Atropine produces its chief therapeutic effects by depressing certain nerve-endings the majority of which belong to the para-sympathetic system. It also tends to stimulate some nerve-centers but, except when large doses are taken, this action is not very obvious.

The centers that are affected are.—1. Cerebral centers, but the higher psychic functions are not stimulated.

2. In the medulla, the respiratory center is stimulated to some extent by moderate doses and the vagus and vaso-constrictor by large doses, but these centers are all depressed by toxic doses. The vasodilator centers controlling the vessels of the skin are, apparently, stimulated by very moderate doses.

3. The spinal cord is stimulated by large doses, but not to anything like the extent that it is by strychnine.

The nerve-endings depressed by atropine are: 1. The ends of the third nerve in the eye which supply the circular muscle of the irises and the ciliary muscles.

2. Sensory nerve-endings, this action is slight and that upon nerve-endings concerned with the sense of pain is confined to the endings with which the drug comes in contact in considerable amounts, as by local applications.

3. The secretory nerve-endings supplying the secretory cells of the mucous membranes, the sweat glands and the glands which secrete the digestive juices.

4. Motor nerve-endings in the plain muscle tissue of the trachea, bronchi, esophagus, stomach, intestines, spleen,

bile passages, ureters, bladder, urethra, uterus. These motor nerve-endings are not as much influenced as the secretory end-organs.

5. The vagus nerve-endings in the heart.

With the exception of the sensory nerve-endings and those in the sweat glands and uterus, all the endings affected by atropine belong to the para-sympathetic system.

Effects of Local Action.—When atropine is dropped in the **eye** (1) it lessens pain; (2) it acts as a cycloplegic, *i.e.*, it inhibits the contraction of the ciliary muscles and thus prevents the curvature of the crystalline lens which is necessary to see near objects clearly, in other words, atropine *paralyzes ocular accommodation;* (3) it acts as a mydriatic, *i.e.*, it causes dilation of the pupil. When the pupil dilates, the minute openings around its margin are closed and this prevents the escape of fluid from the interior of the eyeball and thus (4) atropine increases intra-ocular tension (the pressure of the fluid within the eyeball). These effects may persist for several days.

When fatty or alcoholic preparations of atropine are applied to the **unbroken skin,** enough of the drug may be absorbed into the underlying structures to slightly depress the sensory and secretory nerve-endings in the part and thus check pain in the area and, when an application is made to the **breasts** during lactation, lessen the secretion of milk. If a large area of skin is kept covered with ointment or a plaster, for a long time, enough atropine may be absorbed by the blood to produce systemic effects, even to cause poisoning.

When it is applied to **surfaces denuded of skin** or to **mucous membranes,** atropine, by its depressant action on sensory nerve-endings, will cause numbness and lessen pain in the area and (as atropine is readily absorbed from such surfaces) the conditions that occur after absorption.

Effects of Actions that Occur After Absorption.—The effects on the **eyes** are similar to those produced by local applications, but they are only obvious when very large doses are taken.

The **secretions**, mucus, sweat, saliva and gastric juice are markedly decreased, but intestinal and pancreatic juices, bile and milk are only slightly diminished, because, it will be remembered, the glands which manufacture these secretions are stimulated by chemic substances formed in the body, to a greater extent than they are by nerve impulses. The secretion of urine is only checked by large doses, but suppression is likely to occur in poisoning.

Even small doses of atropine may check the secretion of saliva and mucus sufficiently to make the **mouth** and **throat** unpleasantly dry and large doses or, sometimes, due to idiosyncrasy, small doses will cause such excessive dryness that swallowing will be difficult and thirst extreme.

As perspiration is checked, the **skin** is dry, also it is warm and, especially that of the face and neck, more or less red, because of the increased amount of blood present as the result of the dilation of the skin blood-vessels.

The depressant action of atropine upon **motor nerve-endings in plain muscle tissue** may overcome spasmodic contractions such as occur, for example, (1) in bronchial muscle, during asthma and whooping cough and, sometimes when breathing is difficult from other causes; (2) in the urinary organs and bile passages when they are irritated by the presence of stones, etc., and in some inflammatory conditions; (3) in the uterus, in some forms of dysmenorrhea; (4) in the intestines, when they are unduly irritated. Nevertheless, atropine, unless taken in large doses, does not reduce the normal tone and contraction of plain muscle tissue to any extent. For example, the normal peristaltic action of the intestines is not actually checked, except by large doses, and the action of cathartics will not, as a rule, be interfered with, in fact, that of those which cause griping may be aided, because the spasmodic contractions which give rise to the sensation of griping often retard the passage of material through the intestine and, therefore, anything that lessens unnatural contractions will facilitate evacuation. The reason why the effects of atropine on motor nerve-endings

is so much more pronounced when there is abnormal contraction is not known.

The heart action is strengthened and somewhat accelerated by atropine, even when the vagus center is stimulated, because, as the vagus nerve-endings are depressed, vagus impulses which, it will be remembered, inhibit the force and rate of contraction, are not readily discharged into the heart muscle and this allows the impulses from the cardiac accelerator center freer play. These impulses, if not in excess, strengthen, as well as quicken, the heart action and a greater amount of blood is thus forced from the heart into the arteries. This causes a rise of blood-pressure and improves the circulation. Apart from this, the only effect of moderate doses upon the blood-vessels is the dilation of those in the skin. Large doses may, possibly, occasionally stimulate the vasoconstrictor center sufficiently to cause contraction of the arterioles in the splanchnic area, but poisonous doses depress the center and cause a fall of blood-pressure. By its action on vagus nerve-endings, atropine will counteract the effect known as *heart-block* which poisonous doses of digitalis produce.

A **rise of temperature** is likely to follow the use of atropine. This, after very large doses, can be accounted for by the increased muscular contractions, induced by the stimulation of nerve-centers, but its cause after moderate doses is not understood, because, though the loss of heat by the evaporation of sweat is diminished, there is increased loss by radiation, on account of the extra amount of blood in the skin. Therefore it is thought that metabolism and, consequently, heat production must be increased due to some unknown effect upon the heat regulating centers.

Breathing is facilitated and generally slightly quickened. This, until recently was attributed to direct stimulation of the respiratory center by the atropine, but it is now thought that this center is only stimulated by fairly large therapeutic doses and that the effect on breathing follow-

ing a moderate dose is due to a slightly relaxed condition of the bronchi. After a large dose, however, the center is stimulated both by the drug and by the extra carbon dioxid that is in the blood as the result of the increased metabolism, but if the dose is excessive, this stimulation is likely to be followed by depression.

The effects of the stimulation of cerebral centers is only manifested after large doses, or in individuals who are easily affected by the drug. It shows in a general restlessness and wakefulness and the patient becomes talkative and, as a rule, rather cheerful, but there is no real intellectual stimulation similar to that induced by caffeine. Poisonous doses will induce delirium and, sometimes, even maniacal excitement. Eventually, if the effects of the drug are not overcome, the centers will be exhausted and stupor and coma will follow.

The effects of the stimulation of the cord, also, is only evident after large doses and is shown chiefly in reflex excitability which promotes twitching of the muscles and, when poisonous doses are taken, convulsions.

Summary of the Principal Effects of a Moderate Dose of Atropine.—Dropped in the eyes; atropine dilates the pupils, increases intraocular tension, inhibits accommodation for viewing near objects. Applied externally, it may have a very slight anodyne effect and, on the breasts, it tends to check the secretion of milk. Taken internally, it checks secretion, especially perspiration, mucus, saliva and gastric juice; it dilates the blood-vessels in the skin and the latter becomes somewhat flushed, warm and dry; spasmodic contractions of the bronchi, urinary and bile ducts, uterus and intestines will be overcome; the heart's action is strengthened and the circulation thus improved; breathing is facilitated and may become deeper and quicker; there may be a slight rise of temperature and a slight dilation of the pupils.

The principal therapeutic uses of atropine are: In the eye, (1) to dilate the pupil in order to facilitate the examination of the interior of the eyeball and, in some

inflammatory conditions of the iris, to prevent or overcome adhesions; (2) to paralyze accommodation when fitting glasses and to enforce the rest of the ciliary muscles; (3) to lessen pain in the eye.

On the skin it is used, generally in the form of ointment, to lessen pain and itching occasioned by some skin affection and ulcers, and, usually incorporated in plasters, it is sometimes used to check pain in underlying, but superficial tissue, but the anodyne action of atropine is very slight, especially when it is applied to the broken skin.

It is applied to the **breasts,** usually in ointment, to check the secretion of milk.

It is applied to **mucous membranes** to lessen pain in the area of its application.

For its effects after absorption it is used: To overcome **spasmodic contractions** of the plain muscle tissue of the viscera, in conditions such as those mentioned on the preceding page. Also it is frequently given with drastic cathartics to prevent griping.

To check **excessive secretion,** for examples: (1) Saliva and mucus, atropine is very frequently given for this purpose before the anesthetics ether and chloroform which, it will be remembered, stimulate excessive secretion); (2) perspiration, as in the night-sweats of tuberculosis; (3) gastric juice when there is hyperacidity and hypersecretion; (4) milk. Also, atropine has been used to check thyroid secretion in exophthalmic goiter, but it is not positively known that it does this, though it does sometimes relieve some of the symptoms.

To facilitate breathing: It is very commonly used with morphine for this purpose in order that the depressant action of the latter on the respiratory center may have less effect. In poisoning by narcotic drugs, atropine is often used in large doses in order to stimulate the respiratory center and, in such case, the symptoms of atropine poisoning must be watched for.

To **stimulate the heart action,** especially when it is abnormally slow.

Toxicology.—People show different degrees of **tolerance** for atropine. Children, as a rule, are less easily affected by it than adults, but some children, as well as adults, have an unknown **idiosyncrasy** which causes even small doses of the drug to produce symptoms of overdosing.

The symptoms of overdosing are: Excessive thirst and such dryness of the mouth and throat that it is difficult to swallow and talk.

The pupils are dilated and ocular accommodation interfered with.

The skin is very dry and red and, sometimes, a rash that resembles the eruption of scarlet fever appears (this is thought to be at least partly due to interference with the circulation in the skin, on account of the dilated blood-vessels).

The pulse becomes increasingly rapid and weak.

The breathing is rapid.

The patient may be sleepless, and restless, and very much excited.

In poisoning, in addition to the above symptoms, there will be twitching of the muscles and, finally, convulsions.

The excitement becomes intense, and delirium, sometimes of a very violent form, is common. This, unless the condition is relieved, is followed by stupor and coma.

The pulse becomes exceedingly rapid and weak, blood-pressure fails and the symptoms of collapse occur.

The temperature may rise exceedingly high.

The breathing becomes slow and shallow and cyanosis is extreme. Death is generally due to paralysis of the respiratory center and consequent cessation of breathing.

The treatment for poisoning includes the general routine described on page 64, for the removal of the drug and the prevention of collapse. The **chemical antidote** is tannin, which, for convenience, is generally given in the form of strong boiled tea. A sedative, such as a bromide, is used to lessen the excitement, but morphine and other drugs which tend to depress the respiratory center are never used, because they would hasten the depression of the center and

this, as previously stated, is the usual cause of death from atropine poisoning. The doctor usually gives inhalations of ether to check convulsions and may prescribe caffeine in the stage of collapse. Artificial respiration is given when necessary.

HOMATROPINE

This is an artificial alkaloid prepared from atropine. Its effects are similar to those of atropine, but weaker. It is used principally as a mydriatic, for which purpose it is often preferred to atropine, because it acts quicker and its effects are not as lasting and, when it is dropped in the eye, it is not as apt to cause systemic effects.

METHYLATROPINE OR EUMYDRINE

This is an artificial compound of atropine. Its action is similar to that of atropine, but weaker, it is, however, somewhat stronger than that of homatropine.

HYOSCYAMINE

Hyoscyamine acts upon the **central nervous system** in the same manner and with about the same intensity as atropine, but its effects upon **nerve-endings** are more pronounced.

As it is difficult to obtain a pure preparation of this alkaloid, it is little used.

HYOSCINE OR SCOPOLAMINE

Hyoscine **acts** upon **nerve-endings** in much the same manner as atropine, but more powerfully.

The effects upon the muscles of the irises and the ciliary muscles develop and pass away more rapidly than when they are induced by atropine.

As a rule, hyoscine, unlike atropine, causes a mild, but prolonged, depression of **nerve-centers**, especially motor and psychic centers, and moderate doses will induce sleep that is likely to last for from 5–8 hours and a

sensation of drowsiness may persist for several hours longer. Hyoscine does not depress the sensory centers very strongly and thus it will not abolish pain, but, due probably to its action on psychic areas, it has a peculiar amnesic effect which causes a patient to forget things, including pain, that occur while under the influence of the drug. Occasionally, especially when large doses are used, hyoscine may cause delirium and excitement in the same manner as atropine.

Due to the depressant action upon nerve-centers, the rate of the pulse is not increased by hyoscine, as it is by atropine.

Hyoscine, even in moderate doses, will sometimes depress the respiratory and vasoconstrictor centers and thus its use is not without danger.

The chief therapeutic uses of hyoscine are: As a mydriatic and cycloplegic.

To quiet restlessness and induce sleep especially in insanity and delirium.

Hyoscine hydrobromide with morphine (commonly referred to as scopolamine-morphine) or with narcophine (scopolamine-narcophine) is employed (1) as a preliminary to general anesthesia, in order to shorten the stage of excitement induced by the general anesthetics and to lessen the secretion of mucus and saliva; (2) as a substitute for general anesthetics in minor operations and obstetrics. It is these preparations that are used in the so-called *twilight-sleep.*

The term twilight-sleep was applied to the use of the above preparations in obstetrics because, in order to favor the action of the drug, the patient's room is kept darkened and the surroundings very quiet. The régime commonly employed is as follows: When the patient is in active labor, upon the physician's direction she is given a dose of either scopolamine-morphine or scopolamine-narcophine; about an hour later, she is given hyoscine alone and this is repeated in smaller doses, at regular intervals of, usually, an hour until the patient does not remember things she

has seen or heard within half an hour. The doses used are only large enough to produce a semi-narcosis. The greatest care is necessary when giving this treatment, in fact, there have been so many accidents, that it is not now used as frequently as it was when first introduced.

BELLADONNA, HYOSCYAMUS, STRAMONIUM, SCOPOLA

The alkaloids atropine, hyoscyamine, and hyoscine are contained in different amounts and in different relative proportions in the crude drugs from which they are obtained (*i.e.*, belladonna, hyoscyamus, stramonium and scopola) and thus there are some differences in the action of these drugs.

The alkaloid in **belladonna** is nearly all atropine and, therefore, its action is that of atropine, though, of course, weaker. The preparations made from the leaves of the plant (deadly nightshade) contain a higher proportion of alkaloid than those prepared from the root.

The principal alkaloids in **hyoscyamus** are hyoscyamine and hyoscine, it contains only traces of atropine, thus it tends to be somewhat narcotic, but, as its alkaloid content is small, only 0.065 per cent., its action is weak. **It is used chiefly** to lessen irritability and contraction of the bladder in cystitis.

Hyoscyamine is the chief alkaloid in **stramonium,** but [redacted]er also contains small amounts of atropine and enou[redacted]oscine to give it a slight sedative effect. It is very frequently used to relax spasmodic contraction of the bronchial tubes, especially in the treatment of asthma, and it is very commonly employed for this purpose as an ingredient of cigarettes and, sometimes, dried leaves of the plants from which stramonium is obtained (the species of the *datura stramonium* or *thornapple*) are set on fire and the smoke inhaled.

The principal alkaloid of **scopola** is hyoscine, but it contains only a small amount and thus the action of scopola is similar to that of hyoscine, but much weaker.

SENSORY END-ORGAN DEPRESSANTS OR LOCAL ANESTHETICS AND ANODYNES

Local anesthetics and *anodynes* are terms applied to drugs which lessen pain by their depressant action on sensory nerve-endings, *i.e.*, receptors, or fibers. The term *anodyne* is used more especially for preparations that are employed as external applications.

Most of the local anesthetics, to be effectual, must be injected under the skin or mucous membrane in such a manner that they will come in direct contact with the end-organs they are to depress, but a few will act if they are applied externally. Ethyl chloride is an important example of the latter

ETHYL CHLORIDE

The origin and nature of ethyl chloride were mentioned in connection with the description of its use as a general anesthetic. When used as a local anesthetic the tube in which the ethyl chlorid is contained is held about 12 inches above the part that is to be anesthetized and the cap of the tube opened. Whereupon, the liquid strikes upon the part and at once evaporates. As heat is necessary for evaporation, it is taken from the area on which the ethyl chloride strikes and the tissue will be frozen in a few seconds, and, cold being a protoplasmic depressant, the nerve-endings in the part lose their sensitiveness. As soon as the skin assumes a white appearance, the tube-cap is closed. Too much ethyl chloride must not be used or the part will be so badly frozen that the tissues will slough. Nobody should attempt to use ethyl chloride until shown how to do so by some one accustomed to using it.

COCAINE

Cocaine is an alkaloid obtained from the leaves of the coca shrub, a plant that is extensively cultivated in the countries of the northern part of South America and to some extent in Mexico and the West Indies.

Preparations and Dosage.—Cocaine, grain ⅛–½ (0.008–0.03 gm.).

Cocaine hydrochloride, grain ⅛–½ (0.008–0.03 gm.). *This is the preparation most commonly employed. The strengths of the solutions generally used are as follows:*

For hypodermic injection, 2–4 per cent.

For use in the eye, ½–2 per cent.

For sprays and swabs on mucous membranes, 2–10 per cent.

For what is commonly known as the infiltration method of administration, the required dose is generally dissolved in 100 c.c. of the diluent that is used.

Fate in Body.—Cocaine is not absorbed from the unbroken skin, but it is readily absorbed from abraided surfaces, mucous membranes, and subcutaneous tissues. Its effects being evident in about 10 minutes. A considerable portion of every dose is destroyed in the body and the remainder is excreted by the kidneys.

Actions.—Cocaine is a general protoplasmic irritant poison. It does not affect the unbroken skin, but solutions over 6 per cent., injected subcutaneously, or those about 20 per cent., applied to mucous membranes, will cause necrosis of the tissue with which they come in contact.

After a temporary irritation, cocaine **depresses** those **nerve-endings** which, when stimulated, give rise to a sensation of **pain**; also, it depresses, though in a lesser degree, the **tactile** nerve-endings (those concerned with the sensation of touch) but it **does not affect** those concerned with the **temperature sense.** If cocaine is put in the nose, it **depresses** the **olfactory** end-organs. When taken by mouth it causes a momentary stimulation of the **taste-buds** connected with the sensation of bitter and then depresses them, but it does not affect other gustatory end-organs.

When cocaine is injected into **nerve-trunks** or the **spinal canal,** it has the same depressant action upon the sensory fibers with which it comes in contact that it has upon end-organs.

Cocaine **stimulates** vasoconstrictor end-organs with which it comes in contact.

After Absorption, Cocaine Stimulates: The cerebral centers controlling the higher intellectual function, those concerned with memory, and imagination, and motor activity; the respiratory vasoconstrictor, and cardiac accelerator centers of the medulla; and the spinal reflex centers. The stimulation, especially that of psychic centers, is likely to be followed by depression.

Large doses will have a direct **stimulant effect upon muscle** tissue, especially plain muscle tissue, but such stimulation is likely to be followed by depression. This effect upon muscle tissue is particularly evident upon that in the irises of the eyes.

Effects of Local Actions.—When cocaine is applied to the **eyes,** or to a **mucous membrane,** or to a **surface from which the skin has been removed,** or when it is **injected** under the skin, a momentary smarting sensation is felt, but this is almost at once followed by abolition of sensation of pain in the part, except when the pain is due to heat, as when the cautery is used; the blood-vessels in the area are so contracted that the tissue becomes bloodless and shrunken, though not to quite such an extent as when epinephrine (adrenaline) is used.

Pain is only abolished as long as the drug remains in contact with the nerve-endings and this, unless large doses are used, will only be about 15 minutes. The blood-vessels, however, remain contracted for a considerably longer period, because of the stimulation of the vasoconstrictor center after the drug is absorbed.

When cocaine is dropped in the eyes, the pupils first contract and then, almost at once, dilate. This is thought to be due to the action of the drug on the radial muscle tissue in the iris, and, probably, after absorption, stimulation of some part of the sympathetic nerve supplying the radial muscle. The dilation may persist for an hour or more.

When cocaine is taken by **mouth,** the bitter taste of the

drug is appreciated for a few seconds, but, after that, bitter substances will not be tasted.

In the **stomach**, the drug, by its depressant action on nerve-endings, lessens irritation and may thus check nausea, vomiting and hiccough. As cocaine is almost entirely absorbed from the stomach, the only effects upon the **intestine** are those that occur after absorption.

The Effects of the Action of Cocaine after Absorption. As the result of the action on the **cerebrum**, the recipient is brighter, memory improved, the ability to reason is increased, the imagination is stimulated, the person is likely to be talkative and somewhat restless. The stimulation is usually followed by depression and the individual feels melancholy and dispirited.

The rate and depth of **breathing** and increased.

The **heart** beats more rapidly, but its action is strengthened and blood pressure is raised. These effects are usually the result of the stimulation of the cardiac accelerator and vasoconstrictor centers but, when large doses are taken, they may be partly due to direct stimulation of the heart muscle and the muscle tissue in the walls of the blood-vessels; however, when doses large enough to stimulate the muscle to these parts are used, their depression is likely to follow and, in such case, the arteries will dilate widely and collapse occur.

The stimulation of spinal centers is largely responsible for the effects upon muscles described in the paragraph following and, in overdoses, it causes muscular twitching and convulsions.

Muscle tone is increased and fatigue lessened, but it is thought that, except when large doses are taken, this is chiefly due to impulses coming from the cord. In South American countries, where the coca shrub is grown, many of the natives chew the leaves and, when they are supplied with these, they can go for days without food and, apparently, not feel hunger or exhaustion, even when doing hard work.

The increased muscle tone of the **intestine** favors peris-

talsis and large doses of cocaine will cause diarrhea but this is likely to be followed by intestinal paralysis.

The excretion of urine is increased as the result of the rise of blood-pressure in the renal vessels.

Cocaine is not used in therapeutics for its effects after absorption, because its favorable ones can be also obtained with caffeine and the latter does not have as many undesirable effects as cocaine. Nevertheless, it is very important for nurses to remember the systemic actions of cocaine, because they occur, sometimes to a very extreme degree, when the drug is used for its local action.

The undesirable effects of cocaine are: (1) the intense psychic depression that frequently follows stimulation. (2) Due to idiosyncrasy, even moderate doses of cocaine will poison some individuals. (3) There is no drug habit that is more easily contracted, nor more difficult to break, than the cocaine habit.

Cocaine is used chiefly: (1) To promote local anesthesia when an incision is to be made. For this purpose it is usually injected hypodermically and, as it only induces anesthesia while it is in contact with the nerve-endings or fibers, some means is usually taken to prevent its absorption. The most common one being to use epinephrine (adrenaline) with the cocaine, for the former contracts the blood-vessels in the area of its application to such an extent that absorption is delayed. When adrenaline is not to be had an ice cap is sometimes applied to the part or, if the part to be operated on is a limb or finger, an elastic bandage is put around the part, just above the point where the incision is to be made in order to limit the flow of blood, and, with it, the anesthetic, from the area. Restricting the absorption of cocaine tends also to lessen the danger of poisoning. Cocaine is sometimes injected into a part that is to be operated upon, even when a general anesthetic is given, in order to, by lessening the stimulation of nerve-endings, reduce the inflow of impulses to nerve-centers for, as previously stated, ex-

cessive stimulation of nerve-centers causes their depression and is thus conducive to shock.

(2) To promote a diffused anesthesia previous to operation. For this purpose, the cocaine is sometimes injected into the nerve-trunk supplying the area that is to be operated upon, or into the spinal canal, or into the tissues in the same way as a hypodermoclysis.

(3) To lessen congestion and sensitiveness in canals (as the nostril, larynx, urethra) in order to facilitate the passage of a speculum or other instrument. For this purpose the drug is generally either sprayed or swabbed over the part or, in the rectum, it is sometimes incorporated in ointment or a suppository.

(4) It is dropped in the eye (*a*) to cause anesthesia for slight operations; (*b*) to dilate the pupils for examination of the eyes when it is desired to avoid causing changes in the accommodation apparatus.

Toxicology.—Symptoms of acute poisoning are: The patient becomes very excited and restless and may become delirious or the excitement may pass into stupor and coma. The pulse becomes very rapid and weak. The breathing is rapid and at first deep, but, eventually, panting or shallow. The throat is dry, but perspiration is likely to be profuse. The pupils become widely dilated. There may be nausea, vomiting, diarrhea, muscular twitching and, finally, convulsions. The patient may complain of various sensations, as of worms crawling upon the skin, this is known as Magnan's sign. Unless the symptoms are relieved—collapse finally occurs and the patient may die either from failure of the heart action or paralysis of the respiratory center. Occasionally, the period of excitation is short and collapse and death occurs almost immediately.

If too strong solutions are dropped in the eye, conjunctivitis and ulceration of the cornea are likely to follow.

The special points in the treatment of acute poisoning are: To keep the patient as quiet as possible and if, as is usually the case, he is anxious about his condition, reassure him. An ice cap is generally kept on the head and the

doctor generally prescribes large doses of bromide to overcome the nervous excitement and muscular twitching.

The Symptoms of Chronic Poisoning.—The individual is particularly bright, cheerful and talkative, while under the influence of the drug, and moody, despondent, and irritable when he does not get his dose. For a long time these may be the only symptoms but, gradually, the harmful effects of the drug upon the nervous tissue interfere with its functioning and then the individual's mental capacity deteriorates; moral sense becomes perverted; and, finally, as the nerve-centers governing the digestive organs and metabolism cease to function normally, gastro-intestinal disturbances become common, and there will be anemia, and emaciation. Also there will be insomnia and, usually, twitching of the muscles and other manifestations of nervous irritability such as the perverted skin sensations experienced in acute poisoning. Insanity is a common sequence.

In addition to the systemic symptoms there will be local ones the nature of which depend upon the way in which the habitué takes the drug. This varies somewhat, for it may be taken by hypodermic, snuffed up into the nose, rubbed on the gums or taken by mouth. A mucous membrane that is frequently exposed to the action of the drug will, in time, become atrophied and ulcerated; and, when the drug is injected hypodermically, necrotic areas may develop at the sites of injection and, as habitués generally grow careless in the matter of asepsis, abscesses are common.

Treatment for Chronic Poisoning.—This consists in the rapid withdrawal of the drug and the isolation of the patient where it will be impossible to obtain it. Hydrotherapy is very commonly used to overcome the nervous symptoms and sleeplessness. Nutritious food, of a kind to appeal to the patient, properly regulated exercise and entertainment are all exceedingly important items of the treatment. For the patient's tissues must be brought to a healthy condition and his mind diverted.

Cocaine Substitutes

In the search for a substance that would be as efficient a local anesthetic as cocaine, without producing its undesirable effects, a number of drugs have been prepared, many of them from cocaine. Of these novocaine and eucaine are probably the most used.

NOVOCAINE

The advantages of novocaine over cocaine are: Its solutions can be sterilized; it produces no irritation of the tissues; it is only about one-third as poisonous as cocaine. Its anesthetic action, however is neither as strong nor as lasting as that of cocaine. One reason for the relative transitory action is that it does not contract the blood-vessels and thus is rapidly absorbed from the area into which it is injected; therefore, if adrenaline (which does contract the vessels) is used with the novocaine this objection may be overcome.

Novocaine tablets of different strengths are sold (between $\frac{1}{3}$ and 3 grains (0.02 and 0.2 gm.) and some contain adrenaline. A tablet is dissolved in sufficient sterile water to make a solution the desired strength. This is generally, about 3 per cent.

EUCAINE OR BETA-EUCAINE

Eucaine or, more correctly, beta-eucaine, of which there are two preparations, a lactate and a chloride, is only about half as poisonous as cocaine and its anesthetic power is about the same. It does not dilate the pupils nor contract the blood-vessels but it has a depressant action on the heart muscle and, thereby, is likely to cause a relatively slow and weak pulse, otherwise, its action is the same as cocaine. Its solutions can be sterilized.

Both beta-eucaine lactate and beta-eucaine chloride are used in solutions of the following strengths:

$\frac{1}{2}$–2 per cent. for the eye.

2–5 per cent. for mucous surfaces, and hypodermic injections.

0.2–1 per cent. for infiltration anesthesia.

Dosage.—Grains ⅛–½ (0.008–0.03 gm.).

TROPOCAINE

Tropocaine is more irritant locally than cocaine, it does not dilate the pupils nor contract the blood-vessels, otherwise, its action is similar to that of cocaine. Its solutions can be sterilized.

Tropocaine is not readily absorbed from mucous surfaces and thus is given only by hypodermic.

Dosage.—½–1 grain (0.03–0.06 gm.) diluted, as a rule to form 3–10 per cent. solutions.

STOVAINE

Stovaine is said to be somewhat less poisonous than cocaine, but is more irritant locally and is thus more prone to cause "hypodermic abscesses." Its local anesthetic effect is about equal to that of cocaine. It dilates blood-vessels. Because of its irritant properties, it is rarely used in the eyes.

Dosage—Grain ⅓₀ (0.002 gm.). This is usually diluted sufficiently to make ½–1 per cent. solutions for hypodermic use. 5–10 per cent. for application to mucous membranes.

ALYPINE

Alypine solutions cannot be boiled and they are irritant locally. Alypine dilates blood-vessels, but it has no effect upon the pupils. Some authorities state that it is as poisonous as cocaine and others that it is less so. It is rarely given by hypodermic.

Dosage.—Gr. ⅛–3 (0.02–0.2 gm.). This is generally diluted sufficiently to make solutions:

½ per cent. for the eye.

1–10 per cent. for mucous membranes.

HOLOCAINE

Holocaine is an artificial alkaloid prepared from phenacetine. Its action is similar to that of cocaine. Some authorities state that it is more, and others that it is less, poisonous. Its anesthetic power is somewhat greater than that of cocaine and it is somewhat antiseptic. It does not dilate the pupils. Its chief use is as a local anesthetic in the eye for which a 1 per cent. solution is employed.

QUININE AND UREA HYDROCHLORIDE

Quinine and urea hydrochloride, as the name implies is a combination of quinine (described page 343) and urea, a synthetically prepared nitrogenous compound with the same chemical structure as the urea in urine.

Quinine and urea hydrochloride is used as a local anesthetic injected hypodermically and as an application to mucous membranes. It is usually dissolved in normal salt solution and strengths from 0.25–3 per cent. are employed.

MAGNESIUM SULPHATE

The use of magnesium sulphate as a local anesthetic was described in connection with its use for intraspinal injections under General Anesthetics.

ORTHOFORM

Orthoform is an ethereal salt or ester of methyl alcohol and amidobenzoic acid. It is used in the form of dusting powders, ointments, lozenges, and the powder is also given in capsules by mouth. It is employed chiefly as an anodyne for painful ulcers including ulcer of the stomach, for hemorrhoids, and to overcome cough (the lozenges).

Orthoform acts as a mild local anesthetic; at the point of its application it is not readily absorbed and thus produces practically no systemic effects.

Dose, 5–15 gr. (0.3–1.0 gm.).

PROPÆSIN. ANESTHESIN. CYCLOFORM

These drugs all have about the same action as orthoform. Propæsin, in addition, contracts mucous membranes. Cycloform is slightly antiseptic.

Dosage.—Propæsin, 5–8 gr. (0.3–0.5 gm.).
Anesthesin, same as propæsin.
Cycloform, 1½–3 (0.1–0.2 gm.).

HYDROCYANIC (PRUSSIC) ACID (HCN)

Hydrocyanic acid is a very volatile, inflammable, colorless liquid. It has a peculiar odor, similar to bitter almonds. It is usually obtained by the decomposition of one or other of its salts but it may be prepared from: The

kernels of certain fruits, such as the cherry, apple, and plum; bitter almonds; bark of the wild cherry; and the leaves of the cherry laurel. It does not exist in these substances preformed, but they all contain certain glucosides, the principal one of which is amygdaline and a ferment which, when the kernels, etc., are macerated in water, changes the glucosides to hydrocyanic acid. Thus the official oil of bitter almonds (amygdala amara) contains 2–4 per cent. HCN and there may be traces of it in some of the other preparations mentioned, all of which contain amygdaline.

Preparations and dosage:

Dilute hydrocyanic acid, (2 per cent.) 2–5 ♏. (0.10–3 c.c.).
Potassium cyanide, 1/12 –1/6 gr. (0.005–0.01 gm.).
Oil of bitter almond, 1 ♏. (0.06 c.c.).
Syrup of bitter almond, 30 ♏. (2.0 c.c.).
Syrup of wild cherry, 1–4 drams (4.0–15.0 c.c.).
Fluidextract of wild cherry, 15–30 ♏. (1.0–2.0 c.c.).

Actions and Effects.—When applied either to the **skin, mucous membranes,** or **raw surfaces,** hydrocyanic acid depresses sensory nerve-endings with which it comes in contact and thereby lessens irritation and produces a sensation of numbness.

If taken by mouth, hydrocyanic acid will inhibit the action of the digestive ferments and **after absorption** it will have the same effect upon those concerned with metabolism, including the oxidases, *i.e.*, those which promote oxidation and, it is thought that the principal results of the drug after absorption are due to this action. The primary result is that the tissues cannot use the oxygen that is in the blood to the normal degree and a condition of partial asphyxia results. This, if not excessive will cause stimulation of the central nervous system, especially the respiratory, vasoconstrictor and vagus centers and, consequently, the breathing increases in rate and depth, the heart action becomes slow and there is a rise of blood-pressure, due to the contracted arteries. If the asphyxia is extreme, as after a poisonous dose, the vomiting center will be stimu-

lated and also the pupil dilator center and reflex centers and the excessive stimulation will be followed by depression.

The syrup preparations are used to allay irritation in the throat and thus check coughing, but, as they only contain minute amounts of the active principle, their value depends chiefly upon the demulcent action of the syrup. The other preparations are rarely used now for they are excessively poisonous. Nevertheless they, and similar compounds, are fairly common causes of **poisoning,** as they are used in a number of industries. Death may occur instantly after the absorption of even minute amounts or it may be preceded by symptoms of asphyxia (see page 97) and collapse (page 63), also there is a typical odor to the breath and vomitus and, on autopsy, from the interior of the body. **The treatment for poisoning** is the same as for other depressants; atropine is given to stimulate breathing.

ACONITE (MONKSHOOD OR WOLFSBANE)

Dosage: Tincture of aconite, 1–4 m. (0.06–0.3 c.c.).
Aconitine, $\frac{1}{400}$–$\frac{1}{100}$ gr. (0.00015–0.0006 gm.).
For external use aconite liniment and ointment.

Actions and Effects: Applied locally, aconite first stimulates and then depresses sensory nerve-endings thereby causing a sensation of tingling followed by numbness. **When the drug is swallowed** the sensory stimulation also induces a reflex flow of saliva and may cause sneezing, coughing, nausea and vomiting. **After absorption,** the chief actions of a moderate dose are stimulation of the respiratory and vagus centers, so that the breathing is quickened and the heart action slowed and weakened and blood pressure thus reduced. For unknown reasons, the temperature may be lowered. After absorption, the sensory nerve-endings may be affected in the same way as by local applications but, except after poisonous doses, less noticeably. Formerly aconite was often used to reduce blood pressure and as an antipyretic, but, at present, its chief use is as a local anodyne. **Poisonous doses** depress the vital medullary

centers and the heart muscle and, therefore, the breathing becomes slow and shallow and the symptoms of asphyxia (see page 97) and collapse (page 63) are pronounced. Also there will be sensations of tingling and numbness. The treatment for poisoning is the same as for other depressants.

DRUGS WHICH DEPRESS SECRETORY END-ORGANS

The Belladonna group of drugs, which have been described and agaricin are the only drugs of importance used for this effect.

AGARICIN

Agaricin is obtained from the *Agaricus*, a white fungus which grows on the European larch tree.

Its active principle is agaric acid.

Preparations and Dosage.—Agaricin $\frac{1}{10}$–1 gr. (0.006–0.06 gm.).

Agaric acid (not official), $\frac{1}{4}$–$\frac{1}{2}$ gr. (0.015–0.03 gm.).

Agaricin is absorbed slowly and its effects are not lasting.

Action.—Agaricin depresses the terminations of the secretory nerves in the sweat glands but, unlike atropine, not those of other glands. It is slightly irritant to mucous membranes but, as a rule, this action is only evident when large doses are taken.

Effects of Action.—The secretion of sweat is checked; in other words, the drug acts as an anhidrotic.

Large doses will cause nausea, vomiting and diarrhea and, if these conditions are pronounced, they will induce symptoms of collapse and, in such case, the anhidrotic action of the drug will be interfered with as, for unknown reasons, sweating is commonly associated with extreme nausea and collapse.

Agaricin is used chiefly to inhibit the night sweats of tuberculosis. Because of its slow absorption and transitory action, agaricin should be administered about 4 to 5 hours before the time that the sweating generally occurs.

MOTOR END-ORGAN DEPRESSANTS

The drugs belonging to this group—curara, conium, gelsemium, nicotine and lobelia—are rarely used in thera-

peutics at present, but some of them are of interest for other reasons.

CURARA

Curara is obtained from various South American trees and is used by the Indians on the tips of their arrows to render them poisonous.

Curara is of interest because it is much used in experimental work in physiological laboratories and the curara action is often referred to in books on physiology, pathology and materia medica. It consists in depressing the myo-neural junctions in the skeletal muscles and thus inhibiting the discharge of impulses into the muscles. This lessens their tone and, in large doses, causes paralysis. Curara was formerly used to arrest convulsions, especially those occurring in tetanus and strychnine poisoning, but when employed in large enough doses to be of value for the purpose, it tended to depress the respiratory muscles and induced asphyxia and, consequently, death.

The venom of the cobra and some other snakes have much the same effect as curara. Such venom can be sucked from a wound with impunity, if there are no abrasions in the mucous membrane and the poison is not swallowed.

CONIUM (POISON HEMLOCK)

This drug is of interest because it was used by the ancient Greeks as a means of killing criminals and it was the poison by which the Greek philosopher Socrates was put to death.

It has a relatively mild curara-like action and, in addition, it tends to depress sensory nerve-endings slightly. It is occasionally used to inhibit spasmodic contractions such as occur in whooping cough. It causes death in the same manner as curara.

Dose of fluidextract 2–6 m. (0.1–0.4 c.c.).

GELSEMIUM

Gelsemium is obtained from the yellow jasmine, a climbing plant of the southern United States.

Dosage.—Fluidextract 1–5 ♏. (0.06–0.3 c.c.). Tincture 10–15 ♏. (0.06–1.0 c.c.).

When applied locally to the eye, gelsemium dilates the pupil by, it is thought, depressing the endings of the third nerve in the iris.

After absorption its actions are similar to those of conium and it tends to lessen neuralgic pains. The cause of the latter effect is not known.

SPARTEIN AND SCOPARIUS

Spartein is an alkaloid obtained from scoparius or broom plant.

Dosage.—Spartein sulphate $\frac{1}{10}$–2 gr. (0.006–0.1 gm.). Decoction of scoparius 1 oz. (30.0 c.c.).

Spartein depresses motor end-plates in the same manner as conium and it also depresses the heart muscle and stimulates vagus and vasoconstrictor ganglia. Because of the effects of its action on the ganglia, spartein was formerly thought to act in the same manner as digitalis and was sometimes used as a substitute. At present it is rarely used, except, occasionally to relax spasmodic contraction of the bronchial muscle in asthma.

TOBACCO. NICOTINE

Tobacco consists of the prepared leaves of the *Nicotiana tabacum*, a plant common in southern countries. Tobacco contains several alkaloids and a volatile oil to which its aroma is due. Its chief active principle, the alkaloid nicotine, is a highly poisonous substance, but when tobacco is smoked, much of the nicotine is changed to pyridine and similar substances which, though their action is the same as that of nicotine, are not as powerful poisons. Also, people who smoke only inhale a small amount of these substances and they soon establish a tolerance for them and thus their action is only marked the first few times that a person smokes.

Actions.—Nicotine irritates the **mucous membrane** with which it comes in contact.

After absorption, it first stimulates and then depresses: the cerebrum; the medullary centers, especially the vagus; and motor nerve-endings, both those in the skeletal muscles and plain muscle tissue.

Effects of Actions.—The secretion of **saliva** and mucus is stimulated by the irritation of the mucous membrane. This action is particularly marked in those not accustomed to smoking and it is partly responsible for the nausea, vomiting and diarrhea that sometimes follow smoking until the person becomes habituated. The irritation of the alimentary canal will be increased if the saliva, which is of course impregnated with the smoke, is swallowed.

As the results of the action of nicotine, etc., **after absorption,** the heart action is, at first slowed and then, as the vagus becomes depressed, quickened, it is also weakened.

Breathing is first quickened and then slowed.

The contraction of the muscles and the muscle tissue of the viscera is increased and then more or less relaxed.

There is transitory psychic stimulation but this is followed by more or less depression so that a smoke has a slight sedative effect on those accustomed to the practice and, in the unhabituated, after the nausea and vomiting subside, a narcotic.

The only **therapeutic use** of nicotine, etc., is to relax the bronchial muscles in asthma. For this purpose, cigarettes containing tobacco and, as a rule stramonium or lobelia, are smoked.

The symptoms of acute poisoning occur as a rule after the "first smoke" and even the habitué may experience them after smoking an unusually large quantity of tobacco. They are: Nausea, vomiting, diarrhea, headache, dizziness, faintness, pallor of the skin, profuse perspiration.

The treatment consists in making the person lie down where he will get pure air. Aromatic spirits of ammonia and similar carminatives will help in overcoming the condition.

Chronic poisoning is likely to result when an individual smokes to excess. The symptoms vary somewhat but common ones are: Derangement of digestion; nervousness which shows in various ways, such as irritability and restlessness; impairment of intellectual ability; rapid heart action and palpitation; chronic inflammation of the throat which may extend through the Eustachian tube to the ears.

LOBELIA

Lobelia is obtained from the Indian tobacco plant. Its active principle, lobeline, is a volatile alkaloid that resembles nicotine in its nature and action.

Preparations and Dosage.—Fluidextract of lobelia, 1–5 ♏. (0.06–0.3c.c.).

Tincture of lobelia, 10 ♏–1 ʒ (0.6–4.0 c.c.).

Lobelia is used to relieve the spasmodic contractions of the bronchial muscle in asthma. The leaves are now more frequently used (as a constituent of cigarettes) than the liquid preparations because poisoning has frequently followed the use of the latter.

The symptoms of **poisoning** are practically the same as those of nicotine. If the poisoning is due to a fluid preparation taken by mouth, the stomach must be lavaged, otherwise, the treatment is the same as described for nicotine poisoning.

DRUGS WHICH STIMULATE PERIPHERAL END-ORGANS

The principal drugs owing their important effects to this action are: Pilocarpine, physostigma, epinephrine or adrenaline, ergot.

PILOCARPUS

Pilocarpus is obtained from the *Pilocarpus jaborandi*, a Brazilian shrub. Its chief active principle is the alkaloid pilocarpine.

Pilocarpus, 20–30 gr. (1.25–2.0 c.c.)
Fluidextract of pilocarpus, 20–30 ♏. (1.25–2.0 c.c.).
Pilocarpine hydrochloride, 1/10–1/2 gr. (0.006–0.03 gm.).
Pilocarpine nitrate, 1/10–1/2 gr. (0.006–0.03 gm.)

Fate in Body.—Pilocarpine is readily absorbed from the skin and mucous membranes. It is excreted by the kidneys, sweat and salivary glands.

Actions.—Pilocarpine acts only after absorption. It then stimulates most of the **nerve-endings** which atropine depresses, *i.e.*, the parasympathetic nerve-endings and the nerve-endings in the sweat glands. Also, it stimulates the motor nerve-endings in the pregnant uterus. The nerves of the sweat glands and the uterus belong, it will be remembered, to the sympathetic system. If the parts which the parasympathetic system supplies cannot be recalled, see the table on page 82. Pilocarpine affects the secretory nerve-endings to a greater degree than the motor or than the vagus supply to the heart.

In large doses, pilocarpine depresses vital **medullary** and **spinal centers.**

Effects of Actions.—**All external secretions,** except bile, urine and milk, are increased. There is lessened secretion of bile, urine and milk, but this is thought to be the result of loss of water on account of the excessive secretion of sweat and saliva. A single dose of pilocarpine may induce the secretion of as much as a pint of saliva and a much larger amount of sweat. In fact, enough water is often lost from the body to reduce the **weight** as much as between 4 and 9 pounds. The loss of fluid from the body will lessen **edema** if this exists.

The activity of the sweat glands induces the flow of an extra amount of blood into the skin vessels so that the **skin** is likely to become somewhat red and the loss of heat from the body by radiation is increased. The evaporation of the extra amount of sweat also increases the loss of body heat and thus the **temperature** tends to be reduced.

The increase of the scalp secretions promotes the growth of **hair.** Unfortunately, the new hair is likely to be lighter in color than the rest.

Especially when the drug is applied directly to the **eyes,** the pupils become contracted and the accommodation apparatus fixed to view near objects. The continued contraction of the ciliary muscles, which this change in accommodation involves, may give rise to a sensation of pain. Intraocular tension, after a preliminary rise, due to increased secretion, is reduced because of the escape of fluid through the spaces of Fontana, which are opened by the contraction of the pupils. This was explained in the section describing the action of atropine on intraocular tension, which is exactly the opposite of pilocarpine.

Large doses of pilocarpine, by promoting excessive contraction of the **muscle tissue of the stomach and intestines,** may cause vomiting and diarrhea, and abortion has followed the use of large doses during pregnancy, because of the contraction of the **uterine muscles.**

Following large doses of pilocarpine there will be an increase of **leucocytes** in the blood. This is thought to be due to the contraction of the muscle tissue of the spleen, which forces leucocytes from that organ into the blood-stream.

The **heart action** is slowed by large doses and, usually, will continue slow, even when large enough doses are taken to depress the vagus center because, in such case, the heart muscle is also depressed. Occasionally, however, the pulse may become rapid after vagus depression, especially when there is much nausea and vomiting. Whether slow or rapid the pulse will be weak.

Breathing is not affected by any direct action of pilocarpine on the respiratory mechanism, except when the drug is taken in large doses, but nevertheless it may be seriously interfered with by the excessive secretion of bronchial mucus. Following large doses there will be additional trouble from the contraction of the bronchial muscle and the aëration of the blood may be imperfect because of this and of the interference with the circulation of blood in the lungs, due to the slowing of the heart action. Thus there is likely to be more or less dyspnea and

a tendency to cyanosis, and there is danger of edema of the lungs. After poisonous doses, as the respiratory center becomes depressed, breathing becomes slow and shallow and death is generally the result of failure of respiration or of asphyxia due to the air-sacs of the lungs becoming filled with fluid (edema of the lungs).

The chief therapeutic uses of pilocarpine are: To cause miosis (contraction of the pupil).

As an ingredient of hair tonics.

To promote diaphoresis (excessive sweating) in order to reduce edema, the way in which it does this is explained in the section describing the action of diaphoretics.

To overcome conditions in the inner ear due to lack of secretion.

It is important to remember that patients receiving pilocarpine must be carefully watched because of the dangers of interference with the respiration and of cardiac depression.

Toxicology:

The symptoms of poisoning are: The pupils are contracted. The pulse is weak and irregular and, usually, slow. The skin is flushed and covered with perspiration. There is also excessive secretion of tears, saliva, and mucus. There will be dyspnea and cyanosis and there is likely to be edema of the lungs. Loud moist râles will be heard being due both to the fluid in the air-sacs and excess mucus in the bronchi and throat.

Muscular twitching and convulsions are likely to occur as the result of the asphyxia, produced by the blocking of the air-tubes and the interference with the circulation in the lungs. As a rule, the patient remains conscious until shortly before death.

Treatment for Poisoning.—The usual means to remove the drug from the stomach and prevent collapse are taken. Caffeine and camphor are very commonly prescribed for the latter purpose. Artificial respiration is given if necessary.

Atropine is the physiological antidote, because it has the opposite action upon peripheral nerve-endings and it

makes breathing easier. (Pilocarpine, however, is useless in the treatment of atropine poisoning because death from the latter drug is due to its central action, which pilocarpine does not antagonize.)

MUSCARINE

The alkaloid muscarine is the active principle of many of the poisonous species of mushrooms. Its action is very similar to pilocarpine, but it induces vomiting and diarrhea in much smaller amounts and, for this reason, it is no longer used as a substitute for pilocarpine, and is only of interest because it is a common cause of poisoning. The symptoms of, and treatment for poisoning are the same as pilocarpine.

PHYSOSTIGMA (CALABAR BEAN)

Physostigma is procured from the seeds of the *Physostigma venenosum* or *Calabar bean,* a vine which is indigenous in Western Africa. It is of special interest because it was used by the natives of the countries in which it grows as a means of deciding the guilt or innocence of those accused of crime. The accused were made to eat the paste and, if they died, they were deemed guilty; if they survived, they were declared innocent.

The alkaloid eserine or physostigmine is the *active principle.*

Preparations and dosage: Extract of physostigma, $\frac{1}{8}$–1 gr. (0.008–0.06 gm.)

Tincture of physostigma, 15–40 m. (1.0–2.50 c.c.).

Eserine salicylate, $\frac{1}{60}$–$\frac{1}{30}$ gr. (0.001–0.002 gm.).

Eserine sulphate, $\frac{1}{60}$–$\frac{1}{30}$ gr. (0.001–0.002 gm.).

Fate in Body.—Eserine is very rapidly absorbed into the blood from mucous membranes and subcutaneous tissues, its effects being evident in from 15 to 30 minutes. A considerable portion of each dose is destroyed in the body and all that is not destroyed is rapidly eliminated, chiefly in the urine, but, to some extent, in the saliva and bile.

Action:

Physostigmine or eserine acts only after absorption. Its action is similar to that of pilocarpine, but it stimulates some nerve-endings that pilocarpine does not affect and, it is thought, physostigmine does not actually stimulate the nerve-endings, as pilocarpine does, but renders them more efficient in transmitting impulses descending the efferent fibers; the effect, however is that of stimulation. The **nerve-endings** thus acted upon are:[1]

(1) The **secretory nerve-endings** in the sweat, lachrymal, salivary, gastric, intestinal glands, the pancreas, and the secretory cells of the mucous membranes.

(2) The endings of the third nerve in the irises and the ciliary muscles of the eyes.

(3) The motor nerve-endings in the plain muscle tissue of the bronchial tubes, the stomach, intestines, spleen, ureters, bladder, uterus and, unlike pilocarpine, physostigmine acts, it is thought, upon the vasoconstrictor nerve-endings, because the arterioles become contracted. The action of physostigmine on the nerve-endings of the intestinal muscle is particularly marked.

(4) The vagus nerve-endings in the heart; this action is very slight.

(5) The motor end-organs in the skeletal muscles (pilocarpine does not affect these nerve-endings).

Large doses depress the heart muscle and first stimulate and then depress the vital medullary centers, and the reflex centers of the cord, but the psychic centers of the cerebrum are not directly affected by the drug.

Effects of Actions:

When **dropped in the eye** and, though **to a less extent,** when taken internally, eserine causes contraction of the pupils and the ciliary muscles. As the result of the latter action, the lens becomes more convex and the eye is thus accommodated for viewing objects near at hand. The contraction of the pupil widens the spaces of Fontana and

[1] The students should be required to state which of these nerve-endings are not affected by pilocarpine.

thus facilitates the escape of intraocular fluid and thus intraocular tension is lessened. Physostigmine opposes the action of atropine upon the eyes to an even greater extent than pilocarpine.

As the result of the action of the **secretory nerve-endings,** there is increased secretion of tears, saliva, gastric, intestinal and pancreatic juices; perspiration and mucus, but the increase of secretions is not nearly as pronounced as when pilocarpine is used, because physostigmine, by contracting the arterioles in the glands, lessens the blood supply in the glands and this interferes with secretion.

The **heart** beats more slowly and, due to the contraction of the arterioles, **blood pressure** is raised, thus the **pulse** tends to become relatively slow and strong.

The rate of **breathing** is increased by small doses, in the endeavor to overcome the interference with the passage of air promoted by the contracted bronchi, but, following large doses, breathing may become slow and weak as the result of depression of the respiratory center.

There is increased contraction of both **plain and striated muscle tissue.** After moderate doses, this is most evident in the intestinal muscle for physostigmine, whether given by mouth or hypodermic, will increase peristalsis sufficiently to have a cathartic action and it is valuable in overcoming intestinal paralysis. Following large doses there is likely to be twitching of the muscles of the face and limbs, and, after poisonous doses, there is extreme muscular weakness resulting from the depression of the reflex centers and the motor end-organs.

The chief therapeutic uses of eserine are: To reduce intraocular tension in glaucoma and to counteract the effect of atropine on the pupil and accommodation apparatus of the eye. As a cathartic.

Toxicology:

Symptoms of poisoning are: Nausea, vomiting and diarrhea associated with intense abdominal cramps. Slow, weak, irregular pulse and slow, labored breathing with consequent cyanosis. Contracted pupils. Twitching of

the muscles and extreme loss of muscular power, beginning in the legs and ascending gradually upward. Excessive secretion of saliva and sweat. Death is very likely to occur from interference with breathing.

The treatment is the same as for pilocarpine poisoning.

EPINEPHRINE OR ADRENALINE

Epinephrine, commonly known as adrenaline, is an alkaloid obtained from the suprarenal capsules of cattle, sheep or pigs. It is thought to be the same as the internal secretion manufactured by the human glands.

Preparations and Dosage.—Dried suprarenal gland, 4 gr. (0.25 gm. adrenaline).

Epinephrine chlorid, (1:1000 solution) 5–30 m. (0.3–2.0 c.c.).

Adrenaline tablets each contain $\frac{3}{200}$ gr. (0.001 gm.) of adrenaline borate. A tablet dissolved in 15 m. (1.0 c.c.) of water will make a $\frac{1}{1000}$ solution.

Also there are a number of proprietary preparations, some of them synthetic, that are known by various names as *supracapsuline, adnephrin,* etc. And there are preparations of adrenaline for local use in ointments and suppositories.

Fate in Body.—Epinephrine does not penetrate the skin at all, it penetrates mucous membranes slightly, but it is not absorbed, and it is thought that its absorption is inhibited because it constricts the blood-vessels in the parts with which it comes in contact and some investigators believe that, when epinephrine is taken by mouth, it is digested by the gastric juice. When injected into the tissues it is absorbed by the blood, but slowly, for when given in this way, its effects will only be obtained in about half an hour, while, when it is injected into a vein, results will be observed in from 5 to 10 minutes. What becomes of adrenaline after it is absorbed is not definitely known, but, it is thought, it is rapidly decomposed because it is rarely found in the urine or other excreta and its effects are very transitory.

Actions.—Adrenaline has no effect upon the unbroken **skin.** When applied to **abraded surfaces or mucous membranes,** it penetrates as far as the superficial blood-vessels and stimulates the myoneural junctions of the vasoconstrictor nerve-endings.

When adrenaline is dropped into the **eyes** and, to some extent, when it is injected into a vein, it stimulates the myoneural junctions of the sympathetic nerve-endings in the radial muscles of the irises.

When adrenaline is **injected into the tissues or a vein** it stimulates the myoneural junctions of the sympathetic end-organs and the results, except those upon the secretory glands, which are less marked, are the same as when the sympathetic system is stimulated by natural causes. These are described on pages 80 to 82 and, if they are not remembered, the description should be studied before considering the effects of adrenaline action.

Effects of Actions.—When applied to **abraded surfaces** and to **mucous membranes,** epinephrine acts as an astringent, causing such contraction of the local arterioles that the part is rendered bloodless and, consequently, the tissues become white and shrunken and superficial bleeding is arrested. As the effects of the drug on the vasoconstrictor wear off, however, excessive contraction of the vessels is likely to be followed by an abnormal degree of relaxation. For this reason, it is necessary to watch for hemorrhage after adrenaline has been used during operations on mucous-lined cavities, as the nose and throat. For the same reason, though an application of epinephrine will cause temporary relief in the congested conditions characteristic of acute rhinitis and hay fever, the congestion is likely to be intensified later.

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tion and intravenous injections, the pupils become dilated, because of the retraction of the irises, brought about by the stimulation of the sympathetic endings in the radial muscles.

After the drug is absorbed it causes contraction of most arterioles that are supplied with vasoconstrictor nerves, but the splanchnic vessels (those in the abdominal viscera) are contracted to a much greater degree than others and thus more blood is forced into the vessels in the muscles, heart, lungs and brain.[1] The extra amount of blood forced to these parts, especially the brain, is of great value in overcoming the conditions of shock, but, under some abnormal conditions mentioned in a subsequent paragraph, it may have bad effects.

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The rate of the heart action is, at first increased, because of the stimulation of the myoneural junctions of the sympathetic (accelerator) end-organs in the heart, but the rate is soon slowed because the rise of blood pressure induced by the vasoconstriction stimulates the cardiac endings of an afferent branch of the vagus and this, of course, carries impulses to the vagus center. Therefore, after a brief acceleration, the pulse becomes relatively slow, though stronger.

The effects of adrenaline on the plain **muscle tissue of the** viscera coincides with the effects of sympathetic stimulation from other causes; viz., the movements of the stomach and intestines are inhibited, but the contraction of the pylorus and anus sphincters is increased; uterine contractions are stimulated; the muscle tissue of the bladder and that of the bronchial tubes and associated parts relaxed.

A valuable characteristic of adrenaline's action on myoneural junctions is that it affects those of muscle tissue that is in an abnormal state to a greater extent than those of tissue in a normal condition; for example, if the bronchial muscle tissue is contracted, as in asthma, a dose of

[1] The vessels of the heart, lungs and brain, it will be remembered, are so little influenced by the vasoconstrictor mechanism that some investigators consider that their nerve-supply is not connected with the vasoconstrictor centers.

Actions.—Adrenaline has no effect upon the unbroken **skin.** When applied to **abraded surfaces or mucous membranes,** it penetrates as far as the superficial blood-vessels and stimulates the myoneural junctions of the vasoconstrictor nerve-endings.

When adrenaline is dropped into the **eyes** and, to some extent, when it is injected into a vein, it stimulates the myoneural junctions of the sympathetic nerve-endings in the radial muscles of the irises.

When adrenaline is **injected into the tissues or a vein** it stimulates the myoneural junctions of the sympathetic end-organs and the results, except those upon the secretory glands, which are less marked, are the same as when the sympathetic system is stimulated by natural causes. These are described on pages 80 to 82 and, if they are not remembered, the description should be studied before considering the effects of adrenaline action.

Effects of Actions.—When applied to **abraded surfaces** and to **mucous membranes,** epinephrine acts as an astringent, causing such contraction of the local arterioles that the part is rendered bloodless and, consequently, the tissues become white and shrunken and superficial bleeding is arrested. As the effects of the drug on the vasoconstrictor wear off, however, excessive contraction of the vessels is likely to be followed by an abnormal degree of relaxation. For this reason, it is necessary to watch for hemorrhage after adrenaline has been used during operations on mucous-lined cavities, as the nose and throat. For the same reason, though an application of epinephrine will cause temporary relief in the congested conditions characteristic of acute rhinitis and hay fever, the congestion is likely to be intensified later.

When epinephrine is dropped in the **eyes,** it causes contraction of the blood-vessels in the conjunctivæ; thus this membrane becomes shrunken and white (the blood being squeezed from the vessels) and, as the result of the shrinking, the eyelids become retracted, which makes the eyeball appear more prominent. Both from local applica-

tion and intravenous injections, the pupils become dilated, because of the retraction of the irises, brought about by the stimulation of the sympathetic endings in the radial muscles.

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epinephrine that will relax it will have very little effect upon blood-vessels that are in a normal condition and, on the other hand, when blood-vessels are relaxed, contraction will be brought about without any pronounced effects upon bronchial muscle that is in a normal state.

Secretion is not as much influenced by adrenaline as it is by ordinary stimulation of the sympathetic system; it is thought that this may be because the drug induces a greater degree of vasoconstriction. There is however some increase of saliva, mucus and tears. The excretion of urine is at first inhibited, due to contraction of the renal vessels, but later, increased, for the renal vessels relax sooner than the splanchnic and thus more blood is forced into them and, as stated in the section on diuretics, the degree of blood pressure in the renal vessels is one of the most influential factors in regulating the excretion of urine. After adrenaline has been administered slowly in an intravenous infusion, glucose is likely to be found in the urine. This is thought to be due to the stimulation of the sympathetic nerve-endings in the liver which control the change of glycogen to glucose.

The more common therapeutic uses of adrenaline are: It is applied to mucous membranes and abraded surfaces to: Check bleeding and to cause shrinking of the tissues as, for example, in the nasal cavities, to facilitate the insertion of a speculum or other instrument.

It is injected with local anesthetics to, by contracting the blood-vessels in the area, retard the absorption of the anesthetic and thus keep it where it is required and lessen the danger of its causing poisoning.

It is used in intrauterine douches and in irrigation of other cavities, as the bladder, to check local hemorrhage.

It is given as an intravenous infusion to cause a rise of blood pressure and thus act as a circulatory stimulant.

It is given by hypodermic injection to cause dilation of overcontracted bronchi.

It is sometimes used when the suprarenal capsules are diseased.

Bad Effects that Sometimes Follow the Use of Epinephrine.—The continued local use of adrenaline on mucous membranes, as, for example, to relieve congestion in the nose, may induce a chronic congestion.

After a local application or injection, the contraction of the arterioles in the part is likely to be followed by their dilation and, if there is any reason for it, hemorrhage.

Especially when the drug is given intravenously, it may, by contracting the majority of blood-vessels, cause a harmful degree of pressure in the cerebral and pulmonary vessels, which are not contracted, and, if any predisposition exists, it may thereby induce cerebral or pulmonary hemorrhage or edema of the lungs. Also, especially if an intravenous injection is given quickly, the sudden rise of blood-pressure (due to the contraction of the arteries) may offer more resistance to the heart than it can stand, thus precipitating heart failure. Occasionally, for some and unexplained reason, an injection of adrenaline is followed by nervous excitement and restlessness.

Thus, though there is no drug that will cause a rise of blood pressure more rapidly and thereby overcome conditions existing in shock and collapse, the use of adrenaline is not without danger and patients to whom it is given must be watched, and adverse symptoms reported to the physician at once.

Toxicology:

The symptoms of, and treatment for poisoning by adrenaline, are the same as those of collapse, as described on page 63. In addition there may be symptoms of some special untoward action, such as the symptoms of apoplexy (cerebral hemorrhage) or moist râles indicating pulmonary edema.

ERGOT. ERGOTOXIN. TYRAMINE. ERGAMINE

Ergot is a parasitic fungus that sometimes grows on rye and very occasionally, on other grains and even other plants.

It contains several alkaloids and other chemical substances some of which are similar to those formed in putrefying meat, but the only ones that are of importance from a therapeutical standpoint are the alkaloids ergotoxin, tyramine and ergamine.

Preparations and Dosage.—Ergot, 15–60 grs. (1.0–4.0 gm.)

Extract of ergot, 4 grs. (0.25 gm.)

Fluidextract of ergot, 1–2ʒ (4.0–8.0 gm.)

Alkaloids of ergot:

Ergotoxin, $\frac{1}{100}$–$\frac{1}{50}$ gr. (0.0006–0.0012 gm.)

Tyramine, ½–1 gr. (0.03 0.06 gm.)

Non-official preparations of ergot:

Ergotole, 5–30 m. (0.3–2.0 c.c.)

Purified extract of ergot or Bonjean's ergotin, 3–8 grs. (0.2–0.5 g.)

Ernutin by mouth, ½–1ʒ (2.0–4.0 c.c.); by hypodermic, 5–15 m. (0.3–1.0 c.c.)

Cornutol by mouth, ½–1ʒ (2.0–4.0 c.c.); by hypodermic 15–30 m. (1.0–2.0 c.c.)

The new preparations of ergot, which are still non-official, are less irritant locally than the older ones, except the alkaloids.

Fate in the Body.—Ergot and its active principles are readily absorbed from the stomach and intestines and subcutaneous tissues, their effects being evident in about half an hour after a dose is taken by mouth. Their fate after absorption and the channel through which they are excreted are not positively known, but they are thought to be excreted in the urine.

As there are some differences in the actions of ergot's active principles, its action is not quite identical with that of any of its active principles.

Actions.—In the **mouth,** ergot has an unpleasant flavor. It is irritant to **mucous membranes and raw tissues,** but its active principles—ergotoxin, tyramine and ergamine—are not.

When injected **subcutaneously,** ergot and tyramine

stimulate the myoneural junctions of the vasoconstrictor nerves with which they come in contact and ergot also causes irritation.

After absorption, ergotoxin and tyramine produce their effects chiefly by stimulating the **myoneural junctions of** some of the **sympathetic nerve-endings,** especially those in the blood-vessels, heart, uterus, stomach and intestines; thus their action is somewhat similar to that of adrenaline, but there are some points of difference, viz., (1) adrenaline stimulates inhibitory and motor myoneural junctions almost equally and ergotoxin only stimulates the junctions of motor nerve-endings and, though tyramine stimulates both inhibitory and motor, its action upon the motor-endings is very slight; (2) neither tyramine nor ergotoxin act as quickly nor as powerfully as adrenaline, but (3) their effects last longer. In large doses, ergotoxin paralyzes the myoneural junctions which it stimulates. Ergotoxin stimulates the muscle tissue of the iris.

Ergamine acts directly upon unstriated muscle cells and its action varies, not only in different species of animals, but on the tissue of different organs in the same animal. It has a slight stimulant action on the heart muscle and on that of some blood-vessels, especially those of the lungs and heart, but nevertheless, by some unknown action it sometimes causes dilatation of the peripheral blood-vessels and a fall of blood-pressure. It stimulates the uterine muscle. It has a slight stimulant effect upon the bronchial muscle and upon that of the stomach and intestines.

The action of ergot, of course, combines that of all three alkaloids, but it is much less powerful, except perhaps upon the uterus.

Effects of Local Action.—When ergot is **injected into the tissues** it causes irritation and a moderate, but prolonged, constriction of blood-vessels in the area. By these means it sometimes induces local necrosis of the tissue and it is conducive to abscess formation.

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as tingling and itching of the skin and convulsions. The usual symptoms of collapse, brought about by the fall in blood pressure resulting from the direct action of the drug after absorption (chiefly the paralysis of the vasoconstrictor junctions by ergotoxin) and to the vomiting.

The treatment for poisoning consists in lavaging the stomach and taking means to avert collapse.

Chronic poisoning has never been common in this country. It is nearly always due to eating food prepared from infected rye and, until its cause was discovered, it was very common indeed among the poor in European countries, in which rye is much used. In fact, it is thought, that some of the plagues that occurred in Europe, in early days were ergot poisoning.

There are two types of chronic poisoning one known as the *gangrenous* and the other as the *convulsive* or *nervous*.

In the gangrenous form, as the name implies, parts of the body become gangrenous and atrophied. The limbs are most frequently affected, but the eyes, and even the internal organs, are sometimes involved. The fingers and toes may drop off.

In the nervous type, the predominating symptoms are: Headache, dizziness, progressive mental dullness, itching of the skin and hyperesthesia, painful cramps and contractions of the limbs and, in severe cases, convulsions.

Both forms of poisoning are due to the contraction of the arterioles. In the nervous type it is the vessels of the brain that are chiefly affected and the various symptoms result from the coonsequent injury to the nerve-tissue. Death is the common outcome of severe poisoning.

DRUGS WHICH OBTAIN THEIR PRINCIPAL THERAPEUTIC EFFECTS BY THEIR ACTION ON MUSCLE TISSUE

MUSCLE TISSUE STIMULANTS

PITUITARY EXTRACT

Pituitary extract is prepared from the posterior lobe of the pituitary gland of cattle. Further description of the gland and also of its preparations and uses will be found in the section on Glands and Their Secretions.

Administration.—Pituitary extract is generally given either intravenously, intramuscularly or subcutaneously.

Actions.—These are not well understood but most of the effects of pituitary extract are the result of direct stimulation of **plain muscle tissue and the heart tissue.**

Effect of Action.—The **blood-vessels** are contracted and blood-pressure thus raised. As the drug acts directly upon their muscle tissue and not as adrenaline does, on nerve-endings, the contraction of the blood-vessels is more general than when the latter drug is used, the vessels of the brain, heart, and lungs being included. The vessels of the kidney, however, are dilated, the supposed reason for this will be mentioned later. The contraction of the vessels takes place more slowly than when it is induced by adrenaline and it is not as pronounced, but it lasts longer.

As the result of the contraction of the blood-vessels and stimulation of the heart muscle, the **pulse** becomes slower and stronger.

The stimulation of the **intestinal muscle** increases peristalsis and aids in the expulsion of gas.

The stimulation of the **uterine muscle** will hasten labor and the involution of the uterus after parturition.

In a woman who is nursing her child a dose of pituitrin will be followed by an increase in flow of milk, but the actual amount of milk secreted during the day is not increased and thus, it is thought, that the temporary increase is due to the stimulation of the plain muscle tissue around the glands, the consequent contraction of which forces out the milk.

Ordinarily, the excretion of urine is increased, but in the disease diabetes insipidus, it is lessened. The reasons for these effects are not positively known. Some authorities consider that the cause of the diuresis is the increased amount of blood in the renal vessels, due to their dilation at a time when the other vessels are contracted, but others believe that the pituitary extract irritates and thus stimulates the kidney cells and thereby induces excretion and that the dilation of the vessels is the result of the extra activity of the cells. Whatever the primary cause, the increased pressure in the renal vessels favors diuresis. As autopsies on individuals who have had diabetes insipidus have revealed that the disease is usually associated with some defect of the pituitary gland it is believed that the secretion of this gland may in some way regulate the secretion of urine.

The chief therapeutic uses of pituitary extract are: To expel gas from the stomach and intestines. To hasten labor. To improve the circulation.

HYDRASTIS

Hydrastis will be considered here because its chief therapeutic use is for the effects of its action on the uterine muscle; it has, however, a variety of actions.

It is prepared from the roots of the golden seal or *Hydrastis canadensis.* It contains three alkaloids, *viz.*, hydrastine, berberine and canadine. An alkaloid hydrastinine is prepared from hydrastine and is more efficacious than hydrastine.

Preparations and Dosage.—Fluidextract of hydrastis, 30 m. (2.0 c.c.).

Tincture of hydrastis, 1 ℥ (4.0 c.c.).
Glycerite of hydrastis, 1 ℥ (4.0 c.c.).
Hydrastinine hydrochloride, 1/6 gr. (0.01 gm.).

Actions and Effects.—Hydrastis has a bitter **taste,** due chiefly to its berberine, and produces the same effects as other bitters, see page 52.

When applied locally to mucous membranes it, by some obscure action, has the effect of an astringent, causing local concentration of the tissues and tending, in some cases, to lessen catarrhal inflammation.

After absorption hydrastis has: (1) mild strychnine-like action upon the spinal **cord** and the **medulla,** but large doses quickly depress the medullary centers. (2) It stimulates all kinds of **muscle tissue,** but the consequent contraction is sometimes followed by more or less marked relaxation especially when large doses are used. The uterine muscle, however, is not as readily depressed as others. As the result of these effects, hydrastis tends to cause a slight rise of **blood pressure** and to slow and strengthen the heart action, but its action in this respect is variable and slightly larger doses than the average will cause a fall of blood pressure and weakening of the pulse, and, also, general muscular weakness, incoördination of movement and dyspnea. **Poisonous doses** will induce strychnine-like convulsions and subsequent collapse.

The most valuable effects of hydrastis are due to its stimulant action on the muscle tissue of the **uterus.** As the result of this, the tone of the muscle is improved and subinvolution favored; also, partly due to its action on the uterine muscle and partly to its action on the muscle tissue of the blood-vessel walls, hydrastis tends to check uterine hemorrhage. Hydrastinine effects the uterus more powerfully than hydrastis, but even hydrastinine is not as effectual in checking severe hemorrhage as ergot.

Hydrastis is used occasionally as a local application to mucous membranes to reduce inflammatory conditions. It is used as a bitter tonic, and to check menorrhagia

(abnormally profuse menstruation) and metrorrhagia (uterine hemorrhage). Hydrastinine is more commonly used than hydrastis for the purpose last mentioned.

DIGITALIS AND ITS ALLIES

There are a number of drugs, derived from various plants, the active principles of which are glucosides of similar composition and action to those of digitalis. They are known collectively as the *digitalis allies* or *digitalis series.*

The names of the principal ones are shown in the following list of preparations; there are several others but they are so seldom used it is not necessary to consider them.

The active principles of digitalis are: Digitoxin, digitalin, digitalein. It also contains a saponin, termed digitonin, that is thought to be at least partly responsible for the nauseating action that digitalis sometimes has.

Preparations and dosage:

Digitalis (*purple foxglove*).—Powdered leaves, ½–3 grs. (0.03–0.2 gm.).

Extract, ¼–1 gr. (0.015–0.06 gm.).

Fluidextract, 1–3 m. (0.0–0.2 c.c.).

Tincture, 5–30 m. (0.3–2.0 c.c.).

Infusion, ¼–½ ℥. (4.0–16.0 c.c.).

Unofficial preparations:

Digitalin, $\frac{1}{30}$–$\frac{1}{10}$ gr. (0.002–0.006 gm.).

Digitoxin, $\frac{1}{250}$ gr. (0.00025 gm.).

Digalen, 10–30 m. (0.6–2.0 c.c.). The solution contains $\frac{1}{225}$ gr. in each 15 minims and the tablets each contain $\frac{1}{112}$ gr.

Digipuratum, 1½ gr. (0.1 gm.). *This is digitalis freed of digitonin and other objectionable matter. It is sold in tablet form and in solution and* 1 *tablet, or* 15 *minims of solution, is the equivalent of* 1½ *gr. of digipuratum.*

Digitol, 5–15 m. (0.3–1.0 c.c.).

Strophanthus.

Tincture, 5–10 m.

Strophanthin, 1/150–1/60 gr. (0.0012–0.001 gm.). The *active principle of strophanthus.*

Ouabaïn, 1/30 gr. (0.002 gm.). *This is a crystalline strophanthin obtained from certain species of the Strophanthus.*

Squill (*Scilla or Sea onion*).

Fluidextract, 1–5 m. (0.06–0.3 c.c.).

Tincture, 5–20 m. (0.3–1.3 c.c.).

Syrup, 15 m–1 ʒ (1.0–4.0 c.c.).

Compound syrup, 5–30 m. (0.3–2.0 c.c.). *This contains squill, senega and tartar emetic.*

Mistura Pectoralis (Stokes' expectorant), ½–1ʒ (2.0–4.0 c.c.).

Convallaria (*Lily-of-the-valley*).

Fluidextract, 5–15 m. (0.3–1.0 c.c.).

Convallarin, ½–1 gr. (0.03–0.06 gm.). *This is the active principle.*

Apocynum (Dogbane or Canadian hemp).

Fluidextract, 10–30 m. (0.6–20 c.c.).

Adonis vernalis, (not official).

Fluidextract, 5–10 m. (0.3–0.6 c.c.).

Adonidin, 1/10 gr. (0.005) the active principle.

Administration.—When immediate effects are desired it is usually either digipuratum, digalen, strophanthin or ouabaïn that is given and, as a rule, the drug is then injected into a vein. As a rule the minimum doses are used for intravenous administration. All preparations of digitalis should be well diluted. For administration by mouth between at least 1 and 2 ounces of water should be used. Acids are incompatible with digitalis and its glucosides and, therefore, when taken by mouth, these drugs are generally given about 3 hours after meals when there is not much acid in the stomach.

Digitalis and its Glucosides

Fate in the Body.—These drugs are absorbed, though not readily, from the intestine. Following oral administration, it will be at least 12 hours and, possibly, longer

before the effects of a dose are obtained. When given by hypodermic or intramuscular injection, they will be absorbed more rapidly, but even in these forms of administration, absorption is slow and it may be some hours before systemic effects are observed. Elimination takes place partly through the kidneys, but largely through the intestines. Excretion is very slow and thus cumulative poisoning is not uncommon.

Actions.—Digitalis is irritant to mucous membranes and to subcutaneous tissues, but the active principles, especially digitalin, and the new preparations are decidedly less irritant.

Digitalis has a bitter unpleasant taste.

After its absorption digitalis stimulates the cells of the **muscle tissue of the heart.** This is its most important action and it is because of this that it is classified with drugs that obtain their chief effects by stimulating muscle tissue.

Of the nerve-centers digitalis stimulates the cardiac inhibitory (vagus) center and, in large doses, the vasoconstrictor and respiratory centers, and, sometimes, when there is fever, the heat-regulating center; also, especially when the drug has been taken for some time, it tends to stimulate the vomiting center. Poisonous doses stimulate motor reflex centers and, finally, depress the vital centers.

Also, digitalis stimulates the vagus **nerve-endings** in the heart and tends to retard the transmission of impulses over the auriculo-ventricular bundles (described on page 54) and, in large doses, it tends to stimulate vasoconstrictor nerve-endings.

Effects of actions:

The effects of the local irritant action of digitalis are unfavorable for, due to it, when the drug is **injected into the tissues** it causes local pain and congestion and is injurious to the cells in the area on injection, thus it favors abscess formation. The irritation of the mucous membrane of the **alimentary tract** and the unpleasant

flavor help to cause nausea and vomiting at times, though this effect is chiefly due to stimulation of the vomiting center, and may be induced when the drug is given by subcutaneous or intravenous injections. Occasionally, when digitalis has been taken for some time, it induces diarrhea but it is not known if this is due to the irritation of the intestinal mucous membrane or to stimulation of the vagus, which, it will be remembered, is the motor nerve for the small intestine.

The active principles, especially digitalein and the new preparations are not as likely to produce the above effects as digitalis.

The stimulant action of digitalis upon the heart muscle increases its irritability, *i.e., its sensitiveness and readiness to respond to stimuli*), tonicity (*i.e., state of partial contraction which prepares it to respond to stimuli and prevents its becoming dilated by the pressure of the blood poured into it while it is not in active contraction*), contractility (*its power to contract and force the blood from it*).

When these properties of heart muscle (irritability, tonicity, and contractility) are below par, the heart does not force the blood energetically nor thoroughly into the arteries and thus the circulation through the tissues is retarded and there is likely to be more or less congestion in the veins and, consequently, increased transudation of fluid into the tissues. Nevertheless, owing to the diminished circulation through the lungs and intestines, the tissues will not get their required supply of food and oxygen. Therefore, by its action on the heart, digitalis tends to promote the **nutrition of the tissues,** including that of the heart.

Ordinarily, stimulation of the heart muscle tends to increase **the rate of the heart action,** but the stimulation of the vagus and the retardation of the transmission of impulses over the bundle of His prevents this and the tendency of digitalis is to slow the heart action. This is of particular value to the heart muscle when the pulse has been abnormally rapid because, in such case, for

reasons given in the review of the physiology of the circulation, the heart then gets more nourishment and oxygen.

When the blood-vessels are abnormally relaxed, they tend to return to their normal condition, but otherwise digitalis in therapeutic doses does not, as a rule, induce vasoconstriction. For some unknown reason the blood-vessels in the skin of the face and neck are dilated.

As the result of the improvement in the circulation, the tissues receive a better supply of the various materials they require (food, oxygen, hormones) and thus their condition is improved and the organs are better able to carry on their functions. (2) Venous congestion is reduced and, as a result, the excess fluid in the tissues is absorbed. (3) the excretion of urine is increased. As the diuresis is due to the extra amount of fluid in the blood-vessels (chiefly because of the absorption from the tissues) excretion returns to normal when the dropsy is relieved. Digitalis does not, as might be expected, irritate the kidneys during excretion, unless taken in very large doses, because its elimination is so slow and takes place to such an extent through the intestine that it does not pass through the kidneys in irritant concentrations.

Therapeutic Uses.—Digitalis is used in many types of organic heart disease and also when the properties of heart muscle previously mentioned are below par from other causes, as during fever, following debilitating diseases, and in collapse. For the latter purpose it has to be given intravenously or intramuscularly. Digitalis should not be used in emergency without a physician's prescription, because in some conditions, notably that known as *heart-block*, it is dangerous. It is used as a diuretic when there is edema.

Toxicology.—Acute poisoning by digitalis is not common, but as the drug is so slowly eliminated, cumulative poisoning is very likely to occur if symptoms of overdosing are not watched for.

The symptoms of overdosing are abnormal slowing of the pulse, nausea, vomiting and sometimes diarrhea.

That first mentioned is the most important symptom for some people are nauseated after a very few doses, and slowing of the pulse may be due to interference with the passage of impulses over the bundle of His (heart-block), a very serious condition.

Symptoms of more pronounced stages of poisoning either cumulative or from a single large dose are: Alarming slowing and irregularity of the pulse followed (as over-stimulated the vagus becomes depressed) by tachycardia. Feelings of discomfort and oppression around the heart. Slow deep breathing and, later, dyspnea and cyanosis. There may be convulsions. Muscular weakness becomes profound. Death may result from collapse or from failure of respiration.

The treatment for overdosing is to stop the drug and to keep the patient very quiet, this is most important. If the poisoning is pronounced, sodium bromide is likely to be prescribed in order to check nervous irritability, and also morphine, except when there is dyspnea. Atropine is prescribed to overcome the excessive vagus stimulation. An ice-cap is put over the heart region as the cold sometimes relieves the sensations of discomfort.

THE DIGITALIS ALLIES

Strophanthus acts like digitalis with the following exceptions: (1) It has a very pronounced stimulant action on the muscle tissue of the intestine and is therefore prone to cause diarrhea; (2) Its action upon the heart muscle is about twice as strong as that of digitalis and thus, if the drug is injected into a vein, it will produce effects more rapidly and forcefully than digitalis, but, as it is absorbed even less readily than digitalis, especially from the intestine, and is more rapidly excreted it is not as likely to produce cumulative poisoning.

The active principles, **strophanthin** and **ouabain**, are the preparations used for intravenous injections.

Squill acts like digitalis but its effects upon the heart are less reliable and less powerful. Due, it is thought, to a

pronounced nauseant action it stimulates the secretion of a thin mucus and therefore acts as an expectorant. It is for this effect that it is most commonly used in therapeutics.

Convallaria is less reliable and more toxic than digitalis and is now seldom used.

The other preparations also have not been found reliable and are rarely employed.

MUSCLE TISSUE DEPRESSANTS

NITRITES

The nitrites are salts formed by the interaction of nitrous acid with either an alkali or an organic substance of the alcohol type.

Preparations and Dosage.—Amyl nitrite, 2–5 m. (0.13–0.3 c.c.).

Nitroglycerine (1% alcoholic solution, known also as spirits of glonoin and spirits of glyceryl trinitrate), 1–3 m. (0.06–0.2 c.c.).

Nitroglycerine or trinitrine tablets (non-official), 1–2 tablets (each tablet contains $\frac{1}{100}$ of nitroglycerine).

Sodium nitrite, 1–2 grs. (0.06–0.13 gm.).

Potassium nitrate (saltpeter), this is used in cigarettes with other drugs employed for the relief of asthma.

Spirits of nitrous ether or sweet spirits of niter, ½–1ʒ) 2.0–4.0 c.c.).

Erythrol tetranitrate (non-official), 1 gr. (0.06 gm.).

Mannitol hexanitrate (non-official), 1 gr. (0.06 gm.).

Care and Administration of Preparations.—Old preparations of nitrites should not be used because the compounds are unstable and deteriorate rapidly. This is especially true of the liquid preparations. Nitroglycerine, erythrol and mannitol are explosive and must therefore be handled with care; they should not be brought near heat nor subjected to friction.

Amyl nitrite is given by inhalation, the drug being dropped on a piece of folded gauze or a handkerchief and

held over the nostrils until the desired effects are produced. Amyl nitrite, for convenience, is generally purchased in small thin glass ampules, termed pearls, each one of which contains the number of minims required for a dose. Nitroglycerine is administered both by mouth and hypodermic and the other preparations are given by mouth.

Fate in the Body.—Amyl nitrite is almost instantly absorbed from the lungs and it is also rapidly eliminated through the same organs; thus its effects are observed almost at once but last only about 15 or 20 minutes. Nitroglycerine is also rapidly absorbed, whether given by mouth or hypodermic, and it is likewise rapidly excreted, but through the kidneys. Its effects are observed in 2 or 3 minutes and, as a rule, last about an hour. The other preparations are neither absorbed nor eliminated quite as readily as nitroglycerine. Their effects are apparent in from 5 to 30 minutes and last for about 3 to 4 hours. Sodium nitrate is sometimes partly decomposed by the gastric juice and nitrous acid is then liberated.

Actions.—If nitrous acid is liberated it will irritate the stomach and intestines but, apart from this, the nitrites have almost no **local action** and their therapeutic value depends upon their power, after absorption, to **depress plain muscle tissue.** It is the muscle tissue in the arteries and the bronchial tubes that is chiefly affected. The tissue in the blood-vessels of the limbs is not as much influenced as that in the arteries of other parts.

The nitrites also tend to depress the **vagus center** and to stimulate the **respiratory center.** In poisonous doses they will combine with the hemoglobin of the **blood** and lessen its power to absorb oxygen.

Effects of Actions.—The arteries and, to some extent, the veins become relaxed and dilated, but the vessels in the limbs are not as much affected as those in other parts of the body. Dilation of the vessels when they are in a normal condition interferes with the action of the heart and the circulation of blood, but, when the condition of the vessels is causing an abnormally high blood-pressure,

their dilation lessens the work of the heart and improves the circulation. It also tends to promote a relatively soft and bounding pulse and, combined with the depression of the vagus, to increase the rate of the pulse. Therefore, shortly after the administration of a nitrite, the **pulse** should become comparatively soft, bounding and rapid.

The dilation of the **coronary vessels** relieves the pain of angina pectoris, which is due to spasmodic contraction of the coronary arteries.

The dilation of the blood-vessels causes a temporary disturbance in the **cerebral circulation** and gives rise to a throbbing sensation, and a feeling as though the head were bursting and it induces faintness, dizziness and blurring of the sight. These effects are more marked when amyl nitrite and nitroglycerine are used and are much more pronounced if the drug is taken when it is not required. In any case, however, they are only momentary, but persistent headache is very likely to follow the continued use of any of the nitrites.

The bronchial muscle tissue is relaxed and spasmodic contractions such as occur in asthma may be relieved.

The breathing becomes faster and deeper.

The excretion of urine is usually increased. This is due to the extra amount of blood in the renal vessels and not to any direct effect of the drug upon the kidneys.

Therapeutic Uses.—To lower abnormally high blood pressure such as occurs in nephritis and arteriosclerosis.

To relax the coronary vessels in angina pectoris.

To relax the bronchial muscle in asthma.

Sweet spirits of niter is used as a mild diaphoretic and diuretic. The alcohol and ether contained in the compound accentuate these actions of the nitrite, while, as the nitrite content of the drug is only small, the other nitrite actions are not pronounced.

Toxicology.—The nitrites are so rapidly eliminated that a fatal outcome from poisoning is not at all probable, but overdoses, especially of amyl nitrite, may cause an alarming and distressing condition.

The symptoms are: Intense flushing of the skin, especially that of the face and neck. Headache and a sensation as though the head were bursting. Dilation of the pupils and disturbance of vision. Dizziness. Faintness. Weak, irregular pulse. There may be cyanosis.

The treatment consists in reassuring the patient and keeping her quiet and warm in the recumbent position.

PAPAVERINE

This alkaloid of opium is sometimes used as a substitute for the nitrites. It is described on page 155.

DEMULCENTS, EMOLLIENTS AND OTHER PROTECTIVES

The term demulcent signifies *to smooth* and the word **emollient,** *to soften.* Therefore, as mucous membranes, except, sometimes, those of the lips, rarely require to be softened, but, not infrequently, need to be smoothed, substances used to soothe irritated membranes are classed as demulcents. The skin, on the contrary, especially that of the hands and face, often requires to be softened and, therefore, the fatty substances used on roughened. and irritated skin are classed as emollients. The fixed oils and fats used as emollients will act as demulcents on mucous membranes, except those of the intestines. But in these organs they are changed to soaps, which are irritant. Though classed as emollients both the fixed and mineral oils and fats, when used on mucous membranes, are commonly referred to as demulcents.

In addition to being employed to soothe irritated mucous membranes, **demulcents are used:** (1) to protect membrane from irritating substances as, for example, poisons, either those that have been inhaled or swallowed or those formed in the irritated organ; (2) they are used as diluents for irritating drugs, to prevent them irritating the stomach and thus causing nausea or, when given by rectum, to prevent their expulsion; (3) mucilaginous demulcents are used as diluents to retard the absorption of drugs; and (4) to hold insoluble substances in suspension in water.

Demulcents in common use are: The gums of acacia, slippery elm and tragacanth; Irish moss, starch paste, glycyrrhiza, albolene, syrups, white of egg and milk.

The gums for use in the throat are often combined with volatile oils in the form of lozenges. For use in the

alimentary canal they are employed as mucilages, *i.e.*, they are soaked in water, which they absorb thus forming a gummy paste that, if necessary, is diluted to the consistency of a thick syrup. The usual dose of the unprepared gum is 1–2ʒ (4.0–8.0 gm.) and of the mucilage 2–4ʒ (8.0–16.0 c.c.).

Irish moss is a seaweed found chiefly on the Irish coast, it can be prepared for use in the same way as the mucilages.

Starch paste, for rectal administration, is usually made from cornstarch, a teaspoonful of the starch being used to from 1–2 cups of water, according to the consistency required. The starch is mixed with about 2 tablespoonfuls of cold water and about ½ the required amount of boiling water is then added slowly and the mixture is cooked for five minutes, then the remainder of the water is added and the mixture recooked for five minutes, if over a flame, or fifteen, if in a double boiler. Barley, rice and other starches are very commonly used for oral administration.

Glycyrrhiza or *licorice root* is a bland substance with a pleasant flavor prepared from the roots of certain plants. **The dose** of the extract is 15 grs. (1.0 gm.), of the fluidextract, 30 m. (2.0 c.c.). Glycyrrhiza is also combined with other drugs both for its demulcent and flavoring properties.

Albolene, a mineral fat or oil, is used for local applications to mucous membranes. It is not saponified in the intestine and it does not become rancid, as the organic fixed fats do.

Milk and white of egg are very commonly used for diluting irritant medicines and in the first aid treatment for poisoning by irritant drugs. For the latter purpose they are not as efficient as the mucilages, but they can usually be more readily obtained. When used as a demulcent, white of egg should be swallowed in its natural form or only very slightly beaten.

Syrups are used as ingredients of cough medicines as they tend to allay irritation of the throat.

The emollients in common use are: The vaselines

(*petrolatum*) white and yellow, obtained from petroleum. **The petroleum oils, as** albolene. **Lard** (*adeps*). **Lanoline,** fat obtained from the wool of sheep. **Cocoa-butter,** obtained from the same source as cocoa and chocolate, *i.e.*, the cacao bean, it is a firm solid at ordinary temperatures, but is melted at body temperature and it is therefore very commonly used as a base for suppositories. **Yellow wax** (*cera flava*) prepared from the honeycomb of the bee. White wax (*cere alba*) bleached yellow wax. Ointment (unguentum) this is a mixture of lard and wax, it is used as a base for medicated ointments. **Spermaceti** (*cetaceum*), this is obtained from the head of the sperm-whale, it is used as a substitute for fats and waxes in ointments and cold-creams. **Cold-cream** (unguentum aqua rosa), the cold-cream of the U.S.P., consists of white wax, oil of almonds and borax, scented with rose water, but many of the cold-creams in common use have other perfumes and sometimes spermaceti is substituted for wax. **Pure fixed oils,** such as that of olive, cotton and flaxseed and the fixed oil of almonds (this is not to be confused with the volatile oil of almonds). **Glycerine,** as mentioned under cathartics, abstracts water from tissue and, therefore, though it softens the skin it dries it and is temporarily irritating, to abraded or chapped surfaces.

In addition to softening the skin, **emollients serve** as protectives by, when rubbed into skin that is exposed, as that of the face, protecting it from irritation from the chemical rays of the sun and wind; and, when used on burns, ulcers and sores of like nature, preventing the dressing sticking to the wound; when employed for this purpose the emollient usually contains some additional therapeutic agent, such as an astringent or antiseptic.

The hydrocarbon fats and oils (petroleums) do not penetrate the skin as well as the organic fats and oils and, therefore, are not as effective emollients, but they do not become rancid nor favor the development of bacteria and thus they are of more value to protect the skin around wounds from irritating secretions and antiseptics. They, like

other fats, are not miscible with water and prevent the penetration of secretions, etc. flowing over them.

Other protectives are: The paraffines, the powders mentioned under absorbents, insoluble metal salts such as those of bismuth, zinc, and cerium, and collodion. Of these, the following are the only ones not discussed elsewhere.

The paraffines are solid preparations derived from petroleum. They are melted and sprayed over the surface of ulcers, burns and the like. They quickly become solid and form a protective covering which can be readily lifted and removed without irritating the surface as a dressing which sticks to a wound does. The method of using paraffine for this purpose is described in all modern textbooks of nursing procedure.

Cerium oxalate, the only salt of cerium used in therapeutics, is insoluble in water and it is practically inert, thus it has no action other than that of a protective. When swallowed, it is precipitated on the walls of the stomach and intestines and is only slowly rubbed off and eliminated. In the meantime it protects the mucous membrane of these organs from irritating material which they contain and, in this way, it lessens nausea and diarrhea. Though cerium and bismuth salts have no demulcent action, they are often preferred to the demulcents for use in the alimentary canal when the irritation is due to bacterial products, because the demulcents afford food for the bacteria and favor their multiplication. **The usual dose of cerium oxalate** is 2–15 grs. (0.13–1.0 gm.). It is usually given in a glass of milk.

Collodion is a solution of pyroxylin or *gun cotton* in ether and alcohol. It is used to cover small cuts and surfaces denuded of skin, and punctures. **Flexible collodion** contains a small amount of either camphor or Canadian turpentine and castor oil. The oil makes the film which the collodion forms over a surface more elastic and tenacious. **Styptic collodion** contains tannin 20 per cent. and therefore it has a slight astringent effect and tends to check bleeding in the surface to which it is applied.

ABSORBENTS

Absorbents are used to: (1) Absorb moisture and sebaceous matter from the skin. Those used for this purpose are: Dry starches and various powders such as talcum (magnesium silicate),[1] lycopodium (prepared from the spores of the lycopodium or club moss) and boric acid.

(2) Absorb secretions from wounds. Those used for this purpose are described under astringents and antiseptics.

(3) Absorb bacterial toxins.

(4) Absorb gas from the alimentary tract.

KAOLIN

Kaolin is commonly known as fullers' earth, because it is used by fullers (certain cloth workers) to absorb grease from wool.

Dose for internal use (for adults), 4 ounces (120 gm.). It is generally mixed with an equal amount of either milk or water.

The dose for infants is 1 ounce per day, given in divided doses. When the baby is fed with prepared food, the kaolin is usually given with it, the day's dose being equally divided between the feedings.

As an absorbent, kaolin is used chiefly (1) in intestinal diseases of bacterial origin and (2) in diphtheria, as a local application to the throat. It tends to absorb bacteria and their toxins, as well as gas and secretions. When taken by mouth, as it is not absorbed, it carries off the toxins, etc., in the feces. Also, it forms a temporary coating on the walls of the intestines and protects them from irritation.

[1] Salts of silicic acid and magnesium or aluminum. These salts may be prepared by chemical reactions, but they are also found in certain clays and sand.

Kaolin is generally applied to the throat by means of a powder blower, enough being used to cover the affected parts. Applications are usually made every two hours and, before each one, the throat and, when necessary, the nose are irrigated with a solution of, usually, sodium bicarbonate and sodium borate, a.a., 2 per cent. This removes the previous application of kaolin and, with it, a considerable amount of toxins and bacteria.

Kaolin is also used as an ingredient of what is known as *clay poultice* or *antiphlogistine*, which also contains thymol, peppermint, methyl salicylate, and glycerine and is used as a counterirritant. The value of kaolin for the purpose depends upon its power of, after being heated, retaining the heat for a considerable length of time.

CHARCOAL

Charcoal is prepared from burnt wood and bones.

Dosage: 15–60 grs. (1.0–4.0 gm.).

When used as an absorbent, charcoal is given dry in capsules, because its absorbent power is diminished by dilution.

Charcoal absorbs secretions; gas and, to some extent, bacterial toxins. Its chief use as an absorbent is to relieve flatulence by absorbing gas that is causing distress.

Charcoal is also used to time the passage of food material through the alimentary canal (as an aid to diagnosis, etc.). It answers this purpose because it colors food with which it is mixed and the color is retained by the food residue discharged as feces. Thus the time intervening between the intake and elimination of the food can be determined.

BITTERS

The term bitters is used to include a group of drugs used for the effects of their bitter flavor. Certain substances, such as serpentaria and bitter orange peel contain volatile oil, as well as their bitter principle, and these are termed aromatic bitters. Formerly a large number of drugs were listed under this heading, but the only ones in common use at the present time are gentian, hydrastis, the aromatic bitters mentioned above, cinchona, nux vomica and strychnine. Hydrastis and the three drugs last mentioned, having more important effects, are described elsewhere.

Preparations and dosage:

Gentian, extract, 4 grs. (0.25 gm.).

Gentian, fluidextract, 5–30 m. (0.3–2.0 c.c.).

Gentian, compound tincture, 1ʒ (4 c.c.). *This contains gentian, and the aromatics bitter orange peel and cardamom.*

Compound tincture of cinchona, 1ʒ (4.0 c.c.). *This contains cinchona, serpentaria and bitter orange peel.*

Administration.—Bitters are administered 10 to 20 minutes before meals. As their effects are dependent upon their flavor, nothing must be done to disguise this.

Action and Effects.—Bitters stimulate certain taste buds and thereby induce a reflex flow of saliva and gastric juice and, if the appetite is poor, they tend to improve it. As the result, they aid digestion and may thus have a tonic effect upon the body. The aromatics also stimulate the olfactory nerve-endings and they have a slight irritant action upon the mucous membrane of the alimentary canal, which gives rise to mild carminative effects, as described under volatile oils.

DIGESTANTS

Digestants are chemical substances, known as ferments or enzymes, which aid in the digestion of food. They are obtained both from the digestive glands of animals and from certain plants.

Preparations and dosage of digestants prepared from animal glands:

Gastric enzymes:

Pepsin, 5–10 grs. (0.3–0.6 gm.).

Pepsin, essence of, 1–2ʒ (4.0–8.0 c.c.).

Pepsin, glycerite of, 30 m. (2.0 c.c.).

(*Pepsin is obtained from the membrane lining the stomach of pigs.*

Rennin (rennet). *This is extracted from the mucous membrane lining the stomach of (as a rule) calves.* It is used for the preparation of junket and whey.

Pancreatic enzymes:

Pancreatin, 5 grs. (0.3 gm.).

Peptonizing powder. This contains 5 grs. of pancreatin and 15 grs. of sodium bicarbonate. It is used for peptonizing milk.

Holadin, 3 grs. (0.2 gm.).

Pankreon (tannin pancreatin compound), 5–15 grs. (0.3–1.0 gm.).

Panase, 3–5 grs. (0.2–0.4 gm.).

(*The above preparations contain all the enzymes of the pancreatic juice.*)

Diazyme essence, 1ʒ (0.4 c.c.). *This contains the amylopsin of the pancreatic juice*).

Trypsin, 2–5 grs. (0.12–0.3 gm.).

Administration.—Pepsin preparations are only active in an acid medium and thus they are given during or after a meal and, if the gastric cells are not furnishing sufficient

acid, hydrochloric acid is usually given with the pepsin. Pancreatic ferments on the contrary, are only active in an alkaline medium. For this reason, when taken by mouth, a pancreatic preparation will act only after it reaches the intestine, where the contents are alkaline, and when a pancreatic extract is used for predigesting food or disintegrating tissue, it is used with an alkali, usually sodium bicarbonate.

Actions and Uses.—The most common use of these ferments is to digest foods, especially milk and, for infants, starches, before they are used. However, if the stomach or pancreas fails to secrete sufficient juice the lacking ferments may be given by mouth. The ferments which digest proteins have been considerably used in the treatment of cancer, and for the removal of abnormal membrane, such as that which forms in diphtheria, under the supposition that, as they facilitated the digestion of animal tissue, they would, if injected into cancerous growths or abnormal membrane, promote their digestion in like manner; unfortunately they have not given the results expected.

The ferments are thought to have the same action as those manufactured in the body, viz., rennin coagulates milk. Pepsin digests proteins; the preparations containing all the pancreatic ferments will have trypsin (*which digests proteins*), amylopsin (*which digests starches*) and steapsin (*which digests fats*). Diazyme acts only upon starches and trypsin upon proteins.

The principal digestive preparations obtained from plants are: Extracts of malt and diastase.

Extracts of malt, of which there are a number of different ones on the market, are prepared from barley malt. They are supposed to contain diastase, the ferment which develops in malted barley and gives it the power to change starch to dextrin and maltose. It has been shown, however, that these extracts have very little power of digesting starch, because the ferment is rendered more or less inactive by the heat used in their preparation, but, as

they contain dextrin and maltose, they have considerably nutritive value. They are used chiefly to increase the amount of carbohydrate in milk mixtures for infant feeding and as diluents for drugs such as cod liver oil.

Diastase is a ferment obtained from barley malt. It digests starch and is used chiefly in the preparation of cereal waters and gruels for infants.

ACIDS

The characteristics of acids were described in the section devoted to the nature of drugs.

Acids are classified under two main headings, namely, inorganic acids and organic acids.

INORGANIC ACIDS

Preparations and Dosage.—With the exceptions mentioned, the preparations of inorganic acids provided for internal use are 10 per cent. solutions.

Dilute hydrochloric acid, 5–20 m. (0.3–1.3 c.c.).

Dilute nitric acid, 5–10 m. (0.3–1.3 c.c.).

Dilute nitrohydrochloric acid, 5–15 m. (0.3–1.0 c.c.). *This contains approximately* 4 *per cent. nitric acid and* 15 *per cent. hydrochloric acid.*

Dilute sulphuric acid, 5–15 m. (0.3–1.0 c.c.).

Aromatic sulphuric acid, 5–10 m. (0.3–0.6 c.c.). *This contains sulphuric acid,* 20 *per cent. ginger, cinnamon and alcohol.*

Boric acid, which is a very weak acid, is not used for the same purposes as the others and will be described separately.

Administration.—Acids are prescribed to be taken before or with meals. They should be diluted with at least 2–4 ounces of water and taken slowly through a tube. The tube is used to avoid injury to the teeth, which will be caused by the acid combining with the alkaline material of the latter.

Fate in the Body.—Acids interact with alkaline and protein substances in the stomach and intestines and the soluble compounds formed are absorbed by the blood. As the blood always tends to keep substances that it requires, much of the alkaline material of the salts thus produced is split off before excretion, and retained, and the residue, which consists of acid salts, is eliminated in the urine.

Actions.—Acids abstract water and combine with the proteins and alkaline substances of **protoplasm,** including that of **bacteria.** The potency of their action depends upon their concentration and the nature of the tissue. The dry outer **skin** is less affected than the **soft moist tissues** or than the teeth, which contain a large amount of alkaline material.

When acids are taken by mouth they stimulate those taste-buds which respond to acids.

Acids are too thoroughly neutralized in the intestines and blood to affect the tissues **after absorption,** except, in large doses, those of the urinary organs, but, if taken in excess, they will reduce the alkalescence of the **blood** and render the **urine** so acid that it will irritate, not only the kidneys, but the membrane lining the whole urinary tract.

Effects of Actions—On Bacteria.—Dilute acids act as antiseptics; concentrated acids, as disinfectants.

On the skin, dilute acids have practically no effect, but they cause a slight shrinkage of **mucous membranes** and **raw surfaces,** *i.e.*, they act as astringents.

When taken by mouth, acids, by stimulating the taste-buds, increase the flow of saliva to such an extent that, in spite of their action on mucous membrane, they assuage thirst.

In the stomach, if there is a deficiency of natural hydrochloric acid, **dilute acids** act as a substitute for the latter and, if not taken in too large amounts, they (1) aid in the digestion of proteins, (2) help regulate the passage of food from the stomach[1] and (3) after entering the intestine,

[1] It will be remembered that, normally, acid is only secreted after food enters the stomach and that secreted at once combines with the protein of the food. Thus it is only after the protein has taken up all the acid with which it can combine that there is any free acid in the stomach. As soon as this occurs, the sphincter muscle of the pylorus relaxes and some of the chyme passes into the intestine, but acid has the opposite effect on the intestinal side of the pylorus and therefore, as soon as the duodenal contents are acid, the sphincter closes and remains closed until the acid is neutralized.

by activating the prosecretin[1], they aid indirectly in the stimulation of pancreatic secretion.

If taken in too large amounts, acids delay digestion[2] and interfere with the passage of food from the stomach.

Concentrated acids, by their action on protoplasm, cause tissues, even the skin, with which they come in contact, to become shrunken and hard, and to slough, and they cause pain. In other words, concentrated acids act as corrosives. Sulphuric and nitric acids are more corrosive than hydrochloric. Sulphuric acid causes actual charring of the tissues and forms a black slough. Nitric acid stains tissues to which it penetrates a yellow or yellowish-brown color. Hydrochloric acid causes blisters and white discoloration.

Mineral acids produce practically no effects after **absorption** unless they are taken in large enough amounts to reduce the alkalescence of the blood.[3] In such case, whether taken in concentrated or dilute form, they, by interfering with absorption of carbon dioxid from the tissues, promote more or less marked symptoms of asphyxia. This condition is known as *acidosis*.

[1] A substance called prosecretin is manufactured by certain glands in the intestinal wall. This prosecretin is changed to secretin by acids and the secretin is absorbed and carried by the blood to the pancreas, which it stimulates, thereby increasing the secretion of pancreatic juice.

[2] Pepsin is only active in dilute acid solutions about 0.2–0.4 per cent. The intestinal ferments are rendered inactive by acids.

[3] There is no physiological demand for extra acid in the blood or tissues, because acids are being constantly formed in the tissues as the result of catabolism and all not further oxidized to carbon dioxid and water must be neutralized by the alkaline salts and nitrogenous substances contained in the blood. Diminished alkalescence of the blood, whether due to acids absorbed from the alimentary tract or to defective metabolism, interferes with the passage of carbon dioxid from the tissues into the blood and thus it is most important the normal reaction of the blood be maintained. Normally the blood is about neutral, but it has a small excess of potential alkaline radicles.

If enough acid is taken to irritate the urinary tract, there will be frequent micturition and pain and, if the irritation is pronounced the urine will contain albumin and possibly blood.

Therapeutic Uses.—(Local), a drop or two of concentrated acid is sometimes used to destroy warts or to check local infection.

Dilute acids, especially hydrochloric, are given by mouth when there is not enough acid secreted by the gastric cells and they are also sometimes used to assuage thirst and as antidotes in the treatment of poisoning by alkalies, but organic acids are better for these purposes.

Toxicology.—The symptoms of poisoning depend upon the concentration of the acid. Large amounts of even dilute acid will, for reasons previously given, cause a condition of asphyxia, and will not have any pronounced local effects, but concentrated acids taken by mouth will also cause corrosion of the alimentary tract and the usual symptoms promoted by such action. If the corrosion is severe, death from shock may occur before the effect of the acid in the blood (acidosis) is apparent.

The symptoms due to local action are: Intense abdominal pain, vomiting and diarrhea. There will be blood and shreds of mucus and of membrane in the vomitus and feces and the intense stimulation of nerve-endings, involved in the injury to the tissue, will cause such an inflow of impulses to the centers, that convulsions, followed by collapse, are likely to occur.

The symptoms promoted by acidosis are: Dyspnea, followed by shallow, slow breathing, extreme cyanosis, convulsions, coma and collapse. Breathing is likely to stop before the heart action, because of an insufficient amount of carbon dioxid in the blood to maintain the activity of the respiratory center.

If the vapor of a fuming acid is inhaled, death may be almost instantaneous, because the fumes are so irritant that they are likely to induce asphyxia by promot-

ing spasmodic closure of the glottis and edema of the larynx.

If the patient recovers from poisoning by a concentrated acid, the scar tissue formed as healing occurs is likely to interfere with swallowing and with the action of the stomach and intestines, also, following poisoning by a large amount of acid, whether concentrated or dilute, there may be nephritis, due to injury of the kidney cells.

The treatment for the local effects of acid poisoning consist in (1) giving a mild alkali at once, magnesia is the best, but lime water, soap or wall-plaster can be used in emergency; it is imperative that the acid be neutralized immediately if corrosion is to be avoided. Soda carbonate and bicarbonate and magnesium carbonate are good alkalinizers, but when they come in contact with acid, they liberate carbon dioxid, and the gas thus evolved will distend the stomach and, if it is corroded, may cause rupture. (2) Lavage is usually performed, but must be done with caution, or the tube may perforate the injured wall of the stomach. Caution implies that the tube must be well lubricated and introduced slowly, the water (lime water is used if possible) must also be introduced slowly. (3) Demulcents such as white of egg, oil, cream, milk, are given freely and as soon as possible.

The usual treatment for the prevention of collapse is carried out.

To lessen danger of acidosis, sodium bicarbonate, about ½ ounce in a quart of water, is given by rectum and the doctor is likely to give sodium carbonate solution intravenously.

BORIC ACID

Boric or boracic acid is a very mild inorganic acid formed by the combination of the elements boron and hydrogen. It occurs in nature in considerable quantities, both in the free state and in the form of salts, especially the sodium salt known as *borax* or *sodium borate.*

Actions and Effects.—Boric acid, like other inorganic acids, is astringent and antiseptic, but, as its acid properties are not marked, it is not corrosive, and it is only poisonous when relatively large amounts are absorbed. As the result of its astringent action, boric acid tends to dry surfaces to which it is applied and to lessen local congestion and sensation.

It is used: (1) On the skin, chiefly as a dusting powder, either alone or combined with starch or other powders; (2) on abraded and irritated surfaces in the form of ointment, powder, or solution; (3) as a lotion for the eyes, in the treatment of conjunctivitis, usually in a 2 per cent. solution; (4) for the irrigation of any of the mucous-lined cavities, in the treatment of inflammatory conditions, and of ulcers and similar sores; usually in from 2–4 per cent. solutions.

Preparations of boric acid and the ingredients mentioned, widely used as mouth washes and gargles in normal, as well as abnormal, conditions, are: **Dobell's solution** (*described with the carbolic acid preparations*) **glycothymoline** or **liquor antisepticus** (*boric and benzoic acid, the volatile oils of eucalyptus, peppermint and thyme, and water*); listerine (*boric and benzoic acids, thymol, eucalyptol, the volatile oils of wintergreen and peppermint, alcohol, tincture of baptista and water*).

Boro-glycerine is a preparation of boric acid and glycerine that is used chiefly in the treatment of inflammatory conditions of the vagina and uterus, but also as a local application to other mucous membranes. As glycerine abstracts water from tissue, it adds to the effects of the astringent action of the boric acid.

ORGANIC ACIDS

The organic acids used in therapeutics for their acid properties are citric, tartaric, acetic and lactic.

Citric acid is contained in many fruits, but it occurs in largest quantities in the citrus fruits, viz., lemons, oranges

and grape fruit; **tartaric acid** occurs in grapes; **acetic acid** is prepared in several ways, it can be made from ethyl alcohol or by the fermentation of the same kind of substances used in making ethyl alcohol, because it is the product of the oxidation of this alcohol. Acetic acid is the essential constituent of vinegar. Good vinegar contains 6 per cent. acetic acid. **Lactic acid** is prepared chiefly from lactose—the sugar of milk—but it is also made from other sugars.

Ordinarily, fruit juices containing citric and tartaric acids are used when the effects of these acids are desired and buttermilk, fermented by special strains of bacteria, is used to obtain lactic acid effects. However, the following preparations are occasionally substituted.

Preparations and dosage:

Citric acid, ½–1ʒ (15.0–30.0 gm.). For administration by mouth ½ ounce is used to a glass of water; it is prepared in the same manner as lemonade.

Lactic acid (70 per cent.), 5–30 m. (0.3–2.0 c.c.).

Lactic acid diluted to from 20–50 per cent., usually with glycerine, is used externally.

Acetic acid (36 per cent.), 10–30 m. (0.6–2.0 c.c.).

Acetic acid (6 per cent.), ½–2ʒ (2.0–8.0 c.c.).

For External Use.—Glacial acetic acid (99 per cent.) and trichloracetic acid, a crystalline substance.

Fate in the Body.—The organic acids, like the inorganic, unite with alkaline material in the intestine and are thereby changed to salts. The acetates and lactates are readily absorbed but the citrates and tartrates are not. All the salt absorbed is oxidized to alkaline carbonates and as such excreted in the urine.

Actions and Effects.—Organic acids have the same action on **protoplasm** as the inorganic acids, but, with the exception of concentrated acetic acid, it is much less marked; therefore, though the organic acids will have astringent effects, they, with the exception of concentrated acetic acid and, to a slight degree, concentrated lactic acid, are not caustic.

When taken by mouth, the organic acids, like the inorganic, induce a copious flow of saliva and have about the same effects as the latter upon digestion, but beyond this their actions differ.

In the intestine the citrates and tartrates have a mild laxative action because the salt not absorbed prevents the absorption of the liquid in which it becomes dissolved in the intestine, this is further discussed under saline cathartics, page 265. Lactic acid was for some time believed to inhibit the action of putrefactive bacteria in the intestine, but it is now considered doubtful if it does so to any extent.

As the salts of the organic acids are changed to alkaline carbonates after their absorption, they increase the alkalescence of the blood and decrease the acidity of the urine. Also, they raise the osmotic pressure of the blood and thus induce the osmosis of fluid from the tissues and, as this increases the amount of fluid in the blood-vessels, including those of the kidneys, it favors diuresis.

Citric acid tends to unite with the calcium salts of the blood when it is injected intravenously and this lessens the blood's property of coagulability, because the normal calcium salts are essential for this process.

To Summarize.—Applied locally, concentrated acetic acid and to a slight degree, concentrated lactic acid will destroy tissue. All the acids here considered have an astringent effect upon mucous membrane, though, in dilute solutions, this is not pronounced. They increase the flow of saliva and thus lessen thirst; if not taken in too large amounts, they aid digestion and, especially tartaric and citric acid, catharsis. After absorption they increase the alkalescence of the blood, decrease the acidity of the urine and tend to increase the excretion of urine. Citric acid, injected intravenously, lessens the power of the blood to coagulate.

Fruit juices overcome scurvy and it was formerly thought that this antiscorbutic property was due to their salts and acids, but, investigation has shown that it is due

to chemical substances in the fruit juices, known as vitamines,[1] that aid metabolism.

Therapeutic Uses.—Glacial acetic and trichloracetic acids are used to remove warts and similar growths.

Acetic acid in about 2 per cent. solutions is used as an intrauterine douche to, by its astringent effects, check hemorrhage.

Concentrated lactic acid, up to about 50 per cent., is used for its astringent effects in some abnormal conditions of the throat. Dilute lactic acid is used internally to check intestinal putrefaction but it is considered doubtful if it does so.

Citric acid and tartaric acid, especially, are used to relieve thirst, improve the appetite and aid digestion, and to provide the blood with alkaline material. Citric acid is used, generally in the form of hot lemonade, to induce diaphoresis and thus, by lessening congestion, avert colds, but it is really the hot drink that is responsible for the diaphoresis; however, the tendency of the citrates to induce diuresis adds to the results of the diaphoresis.

Citric acid is injected intravenously to inhibit thrombosis.

Toxicology.—Poisoning is only caused by concentrated acetic acid and, possibly, by large amounts of concentrated lactic acid. The ill effects are due to the local action of the acids on the alimentary tract and, therefore, the symptoms

[1] Little is known of the nature of these substances or of the way in which they produce their effects, but they are contained in all living tissue and fresh food and they are destroyed by a high temperature, by alkalies and nearly all substances used for the preservation of food and by drying. There are thought to be three distinct varieties and a lack of one variety is likely to interfere with nutrition in a manner to cause scurvy, a lack of another predisposes to rickets and of the third, to neurotic conditions such as exist in the disease known as beri-beri. The antiscorbutic vitamine is present in greatest amounts in acid fruits, tomatoes, cabbage and turnips. The antirachitic, in green vegetables, the germs of seeds, potatoes, especially sweet potatoes, carrots, bananas, and the fat and milk of carnivorous animals which feed on such things. The antineurotic vitamine is especially abundant in yeast, the seeds of plants and eggs of animals.

are the same as those induced by the local action of the mineral acids. Also, the **treatment** is the same as that used to counteract the local action of the inorganic acids.

OXALIC ACID

Oxalic acid is an organic acid that is contained in a number of plants and is manufactured for commerce by heating wood shavings with caustic potash or by subjecting carbohydrates to the action of nitric acid. It is not used in therapeutics but is mentioned here because it is such a common cause of poisoning, being taken either in mistake for Epsom salts, the crystals of which it resembles, or with intent to commit suicide.

Oxalic acid has the same corrosive effect as the inorganic acids and, therefore, the **symptoms of poisoning** are similar. Also, the **treatment for poisoning** is the same, except that sodium or potassium compounds should not be used to neutralize the acid, for sodium and potassium oxalates are poisonous. The best neutralizers are the calcium salts, either calcium lactate or calcium chlorid, but lime water, chalk, or wall-plaster can be used in emergency.

ANTACIDS

An antacid is, as the name implies. a remedy that neutralizes an acid.

The body conditions that call for the use of an antacid are: (1) Hyperacidity of the gastric juice; (2) systemic acidosis—this may be the result of the absorption of poisonous amounts of acids or of defective metabolism, as in diabetes, uremia, and chloroform poisoning; (3) hyperacidity of the urine.

In order that a drug may act as an antacid it must be either an alkali or else of a nature to be changed to an alkaline substance in the body.

NON-ALKALINE ANTACIDS.

These are the sodium and potassium acetates, the sodium and potassium tartrates, and sodium, potassium and lithium citrates. The acid ions of these salts are acetic, tartaric and citric.

Preparations and dosage:

Acetates, 10–40 grs. (0.6–2.6 gm.).

Citrates, 10–20 grs. (0.6–1.3 gms.).

Effervescent potassium citrate, ½–1 ʒ (2.0–4.0 gms. *This contains sodium bicarbonate.*

Potassium bitartrate (cream of tartar), 2½ʒ (10.0 gm.).

These salts do not, in their natural form, unite with acids and thus they will not **affect the reaction of the gastric juice.**

After absorption, they are acted upon in the same manner as the salts formed in the intestine from acetic acid and the fruit acids (described in the preceding section, under Organic Acids) and thus they tend to increase the alkalescence in the blood and to decrease the acidity

of the urine. The acetates are the most efficient in this respect, because they are more completely absorbed than the citrates and tartrates. The latter, for reason given under Saline Cathartics, have a slight laxative effect.

Sodium citrate is sometimes added to milk to prevent it forming a hard curd. It does this by its action on the calcium salts for changes in these salts, in either blood or milk, interfere with the clotting properties of these fluids.

ALKALINE ANTACIDS

The alkaline antacids are: The alkaline compounds of (1) the metal elements sodium, potassium and lithium; (2) ammonium; (3) the alkaline earths calcium and magnesium.

SODIUM, POTASSIUM, LITHIUM

These alkaline elements are never found free in nature but their salts are widely distributed, they are especially abundant in sea and mineral waters and in salt beds.

Preparations and dosage:

Sodium hydroxid sticks, for external use.

Solution of sodium hydroxid (5 per cent.), 5–15 m. (0.3–1.0 c.c.).

Sodium carbonate, 5–10 grs. (0.3–0.6 gm.). *Larger doses, in very dilute solutions, are sometimes given by intravenous infusion to patients with severe acidosis.*

Sodium bicarbonate, 5–15 grs. (0.3–2.0 gm.). *Larger doses, up to about 2 oz. per day, are given to patients with severe acidosis. They are then usually given by rectum or intravenously in about 3 per cent. solutions.*

The dosage of potassium compounds and lithium salts is the same as that of the sodium.

Administration.—When the **caustic sticks** are used, as soon as the desired degree of corrosion has been obtained, the area must be washed with vinegar ½ per cent. or other dilute acid. Hydroxids and carbonates must be very well

diluted for internal administration. When an alkali is **used to overcome gastric hyperacidity,** it is sometimes given directly after eating but, frequently, the prescription calls for its administration between one and two hours after a meal, because, as a rule, the acidity of the gastric juice is greatest at this time. Sometimes, when one of the reasons for the use of the alkali is to **liquefy the mucus in the stomach,** the drug is given before breakfast. When an alkali is intended for its effects after absorption, if given by mouth, it is generally administered before meals (while the gastric contents are neutral) in order to prevent its neutralization.

Fate in the Body.—The preparations of the alkaline metals that are used as antacids are readily absorbed through mucous membranes. They are excreted chiefly through the kidneys, but also to some extent through mucous membranes.

Actions.—In addition to neutralizing acids, the alkalies tend to abstract water, saponify fats, and dissolve the albumin of protoplasm with which they come in contact. The degree of their action will be in proportion to their concentration and the nature of the tissue. They affect the soft tissues more readily than the skin. The hydroxids are the most strongly alkaline and the bicarbonates the least.

Effects of actions:

On Bacteria.—Even dilute solutions of hydroxids and carbonates are disinfectant and the bicarbonates are antiseptic.

On the Skin and Mucous Membranes.—Even moderately dilute solutions of the hydroxids will destroy the skin and solutions as dilute as 5 per cent. are destructive to mucous membranes. The carbonates are less caustic and will only destroy the skin if concentrated solutions are kept in contact with it for some time, but even moderately concentrated solutions are destructive to mucous membranes. Under the influence of corrosive concentrations

of these alkalies, the affected parts become soft, swollen and inflamed and then necrosed; a soft crust usually forms over the surface, but drops off in a few days leaving an ulcerated area.

Dilute solutions of the hydroxids and carbonates when applied to the **skin,** dissolve its outer layer of cells and the sebaceous matter on its surface and thus soften and cleanse it, also, they soften dried exudates and crusts and promote an irritation that is sometimes of value in relieving itching such as exists in urticaria. They affect **mucous membranes** in the same way as the skin, but more readily, and they also dissolve **mucus.** Concentrated solutions of the bicarbonates have about the same effects as dilute solutions of the other alkalies except that they, especially sodium bicarbonate, are practically non-irritant and their other properties make them soothing to the skin when it is irritated, as in some forms of erythema, or injured, as by burns.

When they are taken by mouth, these drugs, in addition to their effects on mucous membrane and mucus, lessen the acidity of the gastric juice and promote contractions of the stomach muscle. The carbon dioxid, liberated from the carbonates and bicarbonates when they come in contact with acid, aids in the latter action. As the results of these effects, nausea is likely to be relieved and also pain that is due to hyperacidity of the gastric juice, and gas is expelled. When there is an excess of acid in the stomach, digestion will be aided by the judicious use of an alkali, but, otherwise, the digestion of proteins will be retarded, because the pepsin, which promotes their digestion, is only active in a solution that is about 0.2–0.4 per cent. acid. Some investigators believe that, though these alkalies are effective antacids for hyperacidity due to fermentation, they are not beneficial in the condition known as *hyperchlorhydria* (excessive secretion of hydrochloric acid) because the irritation (due in the case of sodium bicarbonate to the carbon dioxid) stimulates the secretion of hydrochloric acid and also hastens the

passage of the salt from the stomach so that its effect is not as lasting as that of the alkaline earths.

The salts formed in the stomach by the interaction of these alkalies with the acid of the gastric juice are readily absorbed and, therefore, if no more alkali is taken than required to reduce the acidity of the gastric juice to its normal degree, they will have practically no effect in the intestine; except that, if the latter has been irritated by the excessive acidity of the chyme entering it from the stomach, the abnormal conditions induced by the irritation (*e.g.*, catarrh and pain) will gradually subside when the chyme is kept normal. If, however, so much alkali is taken that the chyme is alkalinized, or even neutralized, intestinal digestion will be delayed because some acid is necessary to activate the hormone which stimulates the pancreas.

After their absorption the alkaline salts: (1) Increase the amount of alkaline material in the blood and thus help to overcome the conditions present in acidosis (described under acids); (2) they raise the osmotic pressure of the blood and, thereby, increase the osmosis of fluid from the tissues into the vessels and thus favor increased excretion of urine, as described on page 47; (3) they reduce the acidity of the urine.

Potassium hydroxid and carbonate are said to be more destructive to tissue than the sodium compounds and the potassium ion tends to depress the heart muscle.

Lithium salts were formerly much used in the treatment of gout with the belief that they dissolved urates, but this has been proved an error and they are rarely used at present.

Therapeutic Uses. External.—The caustic sticks are used occasionally to remove warts and similar growths. Solutions of the carbonate and bicarbonate are used as wet applications to the skin and to abraded surfaces to loosen dried exudates and to relieve itching and especially sodium bicarbonate to lessen pain due to burns.

A bicarbonate is often added to solutions for douching

mucous membranes and gargling the throat when there is tenacious mucus present.

Internal.—These drugs, especially sodium bicarbonate, are used to overcome (1) gastric hyperacidity; (2) acidosis; (3) excessive acidity of the urine.

They are used in emergency as antidotes for poisoning by acids but, for reason already mentioned, they should only be given by mouth if other alkalies cannot be obtained and they must be well diluted.

The bicarbonates, especially potassium, are used in expectorant mixtures, because of their effects on mucus.

Toxicology.—The symptoms of poisoning are almost entirely due to corrosion of the gastro-intestinal tract and thus are similar to those produced by the local effects of corrosive acids. The danger of collapse is especially great when the poisoning is due to potassium compounds.

The treatment is the same as for poisoning by acids, except that dilute acids are substituted for alkalies (the organic acids—acetic (vinegar), citric and tartaric are best for the purpose) and alkalies are not given intravenously.

AMMONIA OR AMMONIUM

Ammonia (NH_3) is a gaseous compound of nitrogen and hydrogen. It is derived chiefly from coal, by heating the latter in an appliance from which air is excluded, but it is one of the several compounds of nitrogen and hydrogen produced during the decay of dead animal and vegetable matter.

Ammonia gas is easily condensed to a colorless liquid and can be purchased in this form, but the liquid preparations ordinarily used are solutions of the gas in water.

Preparations and dosage:

For external use:

Ammonia liniment.

Strong ammonia water, this contains 28 per cent.

For internal use:

Ammonia water (*aqua ammonia or spirit of hartshorn*), 10–30 m. (0.6–2.0 c.c.). *This contains* 10 *per cent. ammonia.*

Aromatic spirits of ammonia, ½–1ʒ (2.0–4.0 c.c.).

Ammonia carbonate 5–20 grs., (0.3–1.3 gm.).

Ammonia acetate (*spirit of Mindererus*), 1–4ʒ (4.0–16 c.c.).

Ammonia chlorid 5–20 grs., (0.3–1.3 gm.).

There are also a number of salts, of which ammonia forms the base, that owe their principal properties to their acid ion. They are described under the headings of the more important principle.

The acetate and the chlorid liberate ammonia so slowly that they have not a typical ammonia action and will be discussed separately.

Administration.—For its reflex effects ammonia may be given by inhalation or by mouth. For administration by inhalation the stronger water or smelling salts may be used, the container being held in such position that the gas can be inhaled. Care must be taken when giving inhalations to an unconscious person or intense local irritation may be induced. To neutralize the gastric juice the drug must be given by mouth. For oral administration ammonia compounds should be moderately diluted, if too concentrated, they may cause nausea and vomiting, if too dilute, their reflex effects will be minimized.

Fate in Body.—A portion of a dose of any of the ammonia compounds under discussion will be changed to the neutral salt ammonium chlorid by interaction with the hydrochloric acid of the gastric juice and, as such, absorbed and excreted in the urine and possibly the sputum. All that is not neutralized is changed to urea in the liver and as such excreted through the kidneys.

Actions.—Ammonia acts upon protoplasm in the same manner as the metal alkalies but, owing to its volatile nature, its effects are less enduring and, therefore, less caustic. For this reason it can be used in concentrations that will produce sufficient irritation to induce characteristic carminative reflexes without injury to the tissues. **When given by mouth** it acts like other alkalies upon the acid in the stomach, but **after absorption,** as it passes directly through the portal vein to the liver where, all that has not been neu-

tralized is changed to urea, it does not act as antacid and its effects are due to the presence of the urea and neutral salt—ammonium chlorid—in the blood.

Effects of Action.—On the skin, the only effects, if the ammonia is allowed to evaporate, will be the removal of fat and other soiling matter, and softening of the skin and, possibly, if the solution is concentrated, reddening. If evaporation is prevented, however, blisters will form and the tissue may be destroyed.

Mucous membranes are more easily irritated than the skin and thus when ammonia is taken, either by mouth or inhalation, the irritation increases the amount of blood in the affected membrane and gives rise to reflexes that (1) stimulate the secretion of a thin mucus and saliva; (2) cause the breathing to become quicker and deeper; (3) the pulse to become stronger and, usually, more rapid, though, if abnormally fast at the time, it may be slowed for reasons given on page 55. These effects, like all reflexes, take place almost instantaneously, but they are transitory; however, they are often of value in overcoming conditions that cause fainting.

When the drug is swallowed, in addition to the above effects, it neutralizes acid in the stomach, liquefies mucus and promotes muscular contractions of the stomach and intestines which favor the expulsion of gas. These effects, as well as the reflexes help to overcome nausea, when the drug is taken in moderate doses and dilutions, but too large or concentrated doses will induce nausea and vomiting.

The presence of the ammonia chlorid and extra urea in the blood raises its osmotic pressure and this, for reasons given on page 47, favors diuresis. This is practically the only effect **after absorption,** unless the ammonia is taken in larger amounts than can be neutralized or changed to urea at the time, in which case there may be a temporary stimulation of the heart muscle and medullary centers, followed, if the dose is excessive, by their depression.

Therapeutic Uses.—The liniment and, very rarely, the stronger water are used as external counterirritants.

The gas of liquid preparations is given by inhalation to overcome the conditions causing fainting. The aromatic spirits, carbonate and water, are given by mouth for the same purpose and also, especially the aromatic spirits, to relieve nausea and flatulence and hyperacidity of the gastric juice. The carbonate is used in expectorant mixtures.

Toxicology.—The symptoms of poisoning are the same as those of the metal alkalies with, as a rule, extreme irritation of the throat and upper air passages. **The treatment** also is the same as that for poisoning by other alkalies and, if necessary oil sprays are used to lessen the irritation of the throat.

AMMONIA CHLORIDE

Fate in the Body.—Ammonia chloride is readily absorbed through mucous membranes. It is excreted by ammonia chloride in the urine and, especially when the individual has a cold and the bronchial mucous glands are unusually active, the sputum.

Actions and their Effects.—Ammonia chloride does not liberate ammonia quickly enough to act as an alkali and thus all its effects are due to its salt action. These are: Extraction of water with consequent shrinking of **mucous membranes** with which it comes in contact and irritation. The irritation in **the mouth** increases the flow of saliva and this and the extra water taken from the membrane fluidifies mucus.

The only effect **after absorption is a** tendency to cause diuresis.

AMMONIA ACETATE

This salt has practically no effect until after absorption. It is changed to urea in the liver and therefore it raises the osmotic pressure of the blood and thereby, for reasons already given, increases the excretion of urine and to some extent, of perspiration.

It is used as a mild diuretic and diaphoretic.

THE ALKALINE EARTH ANTACIDS

The alkaline earths used as antacids are, as previously stated, alkaline compounds of magnesium and calcium. Compounds of these elements are very common in nature for they comprise a considerable percentage of the rocks and earth, and they, especially calcium, occur in organic matter and calcium compounds are essential constituents of the human body. Their distribution in the body will be discussed later.

MAGNESIUM

Preparations and dosage of alkaline magnesium compounds:

Magnesium carbonate, 45 grs. (3 gr.).

Magnesium hydroxid (milk of magnesium), 1–3ʒ (4.0–12.0 g.).

Magnesium oxid, 5 grs.–1ʒ (0.3–4.0 gm.).

Important, but non-alkaline, salts of magnesium are magnesium sulphate, described under Cathartics and Anesthetics, and a cathartic, magnesium citrate.

Magnesium compounds, especially magnesium carbonate, are common ingredients of the alkaline mineral waters.

The actions of magnesium antacids differ from those of the alkaline metals in the following respects: (1) Though they combine readily with acids, their other alkaline properties are feeble and thus they are not at all caustic. (2) They and the salts formed from them in the stomach are very imperfectly absorbed and thus their use as antacids is limited almost entirely to the gastric juice. (3) As they prevent the absorption of the water in which they are dissolved, they act as laxatives, the reason for this is stated under Saline Cathartics.

CALCIUM OR LIME

Preparations and dosage:

For external use:

Calcium oxide (unslaked lime).

Lime liniment (Carron oil). *A mixture of equal parts of lime water and linseed or olive oil. It was so named because it was first used at the Carron Iron Works for the first-aid treatment of burns.*

Precipitated chalk, an ingredient of tooth powders.

For internal use:

Calcium carbonate (chalk, cretæ), 10–60 grs. (0.6–4.0 gm.) *This is insoluble in water.*

Chalk mixture, 1–4ʒ (4.0–20.0 gm.). *Calcium carbonate suspended in water by means of gums.*

Compound chalk mixture, 30 grs. (2.0 gm.). *Calcium carbonate, acacia, and sugar.*

Lime water (liquor calcis), 1–4 oz. (30–0–120.0 c.c.). *A saturated solution of calcium hydroxid. As the hydroxid is only very slightly soluble in water, this solution is only about* 0.14 *per cent., i.e., it contains approximately* ⅓ *gr.* (0.02 *gm.*) *to the ounce.*

Syrup of lime, 30–60 m. (2.0–4.0 c.c.). *Contains* 5 *per cent. lime.*

Calcium chloride, 5 grs. 1 oz. (0.3–30.0 gm.).

Calcium lactate, 5 grs.–½ oz. (0.3–15.0 gm.).

There are also a number of salts of which calcium is the base that owe their most important properties to their acid ion.

Administration.—Calcium preparations used to reduce gastric hyperacidity are usually given about one hour after meals. It is the carbonate preparations, the syrup of lime and the hydroxid that are used for this purpose. The relatively soluble salts—the chloride and lactate, which are neutral salts do not serve as antacids, but they are used for their systemic effects. They, especially the lactate, are sometimes given by hypodermic or intravenous injections. In whatever manner the chloride is used it must be well diluted.

Fate in the Body.—Even the soluble salts of calcium, those of food, as well as the medicinal preparations, are absorbed with difficulty. The calcium not absorbed is

eliminated in the feces. That absorbed circulates in the blood and, if there is a deficiency of calcium in the body, as much as is required will, normally, be taken by the parts requiring it. All not utilized is slowly excreted in the urine or back into the intestine.

Actions and the Effects.—Calcium oxide or unslaked lime is only used in therapeutics as a disinfectant for cesspools and the like. It is highly corrosive.

The other preparations have no effect upon the unbroken **skin,** but calcium chloride extracts water from **mucous membranes** and **subcutaneous tissues** and thus is irritant and astringent. The syrup of lime and lime water also have a slight transitory irritant action and they and the carbonates are astringent, because of their tendency to coagulate surface proteins. By these actions, these compounds contract mucous membranes and raw surfaces and lessen the sensitiveness of nerve-endings. The lactate is less irritant than the other preparations.

In the stomach, in addition to their action on mucous membranes, preparations of the **carbonates** and **hydroxids** neutralize the acid of the gastric juice. **Lime water** contains so little lime that it requires about ½ ounce to neutralize 1 minum of hydrochloric acid and, therefore, its antacid effects are very mild.

By their interaction with the hydrochloric acid, the carbonates and hydroxids are changed to calcium chloride and, in this form, enter the **intestine.** A small amount, about 20–40 per cent., may be absorbed, but the greater part is thrown out of solution on coming into contact with the alkaline secretions in the intestine and the precipitate tends to adhere to the wall of the bowel and protects it from irritation by its contents, also, it lessens the irritability of the nerve-endings. Thus calcium salts promote constipation.

As the uses of the medicinal calcium salts after absorption are the same as those of food it will be well to recall the **important physiological uses of calcium in the body.** These are: Calcium is an important constituent of nearly

all body tissues, but it occurs in largest proportion in the bones and the teeth, of which, chiefly in the form of calcium phosphate, it constitutes about 85 per cent. of the mineral matter that is necessary for their rigidity. (2) Calcium is essential for the development of thrombin, one of the substances required for the clotting of blood. (3) It plays an important part in *sealing the blood-vessels, i.e.,* in preventing excessive transudation through their walls. (4) It opposes the action of sodium and potassium salts in the body; this property is especially marked on the heart muscle, the sodium and potassium salts promoting contraction and the calcium relaxation. (5) It is of importance in the regulating of nerve conduction and it lessens nervous irritability. Convulsions and other nervous manifestations are common occurrences when the body's supply is deficient or when the body is unable to utilize calcium, a condition that occurs in certain diseases as rickets, scurvy and tetany.

The chief therapeutic uses of calcium preparations are: Externally, lime water is a common ingredient of lotions used to relieve itching and irritation in eczema, burns and the like. For the latter purpose it is used in the form of Carron oil (a mixture of lime water and olive or linseed oil) as the oil prevents the primary irritation of the lime.

Internally, for local effects, the carbonate preparations and the syrup of lime, but especially the former, are used to lessen gastric hyperacidity when the condition is associated with diarrhea or nervousness; they are also used in the treatment of poisoning by acids. Lime water is added to milk to, by lessening the acidity of the gastric juice, prevent the milk being clotted into a hard curd.

For their effects after absorption, the chloride and lactate are used: (1) To lessen nervous excitability such as exists in chorea, epilepsy, and diseases of the parathyroid glands; (2) to inhibit the response to local irritation, *e.g.* sneezing as the result of irritation by the pollen of plants, as occurs in hay fever; (3) to overcome the depressant action of poisonous doses of magnesium sulphate on the

spinal cord;[1] (4) to favor the clotting of blood when there is a tendency to hemorrhage, as in typhoid fever and scurvy; (5) to lessen the permeability of blood-vessels when there is excessive transudation, as in scurvy.

Formerly calcium salts were much used in the treatment of hemophilia, purpuras, scurvy, rickets and tetany, under the supposition that these diseases were due to deficiency of calcium in the affected tissues, but it is now known that the two diseases first mentioned are almost always due to some abnormality of the blood-platelets and the other diseases are more frequently due to the existence of some abnormal condition which prevents the calcium being utilized by the body than to a deficient supply of calcium. One of the causes of such lack of assimilation is thought to be the defective metabolism of carbohydrates which gives rise to substances that combine with the calcium and unfit it for use by the cells. The defective metabolism, it is believed, is caused by a lack of either some internal secretion or of food vitamines.

[1] It is thought that magnesium sulphate, under conditions mentioned on page 114, enters between the synaptic membrane of afferent neurones of the cord and inhibits the transmission of impulses, and calcium is thought to relieve the condition by displacing the magnesium, not by stimulating the cord.

CATHARTICS

Cathartics are agents that increase and quicken evacuation from the bowels. Before considering their action it will be well to review briefly the physiology of normal defecation.

PHYSIOLOGY OF DEFECATION

Ordinarily, all food material not absorbed is gradually propelled onward through first the small and then the large intestine by the so-called peristaltic action of these organs.

Peristalsis consists in the formation of series of localized rings or waves of constriction below each one of which is a portion of intestine in a relaxed condition. These waves are, ordinarily, the result of nerve impulses coming from centers in the sacral region of the spinal cord, in response to the stimulation of the centers by afferent impulses, started in the intestine by the material entering it. Thus, normally, a wave of constriction occurs as soon as food is forced to a part of the intestine and this wave, in turn, forces the food onward thereby promoting other waves. The material discharged from the small, into the large intestine, is in a liquid condition, water not being as readily absorbed from the small intestine as from the colon, but, after the food residue enters the latter, the water is gradually taken up and thus, if the feces are not evacuated at the normal rate, they become dry and hard, while if they are hurried through the intestine at an unusually rapid rate they will be soft and even watery.

When the feces reach the sigmoid flexure of the colon their passage is temporarily retarded until reflexes are stimulated which pass them onward into the rectum. The necessary reflexes are initiated in various ways but the

more potent ones are (1) the taking of food when the stomach is empty and (2) the first movements of the body after a period of rest as upon arising in the morning.

When material is forced into the rectum the latter is thrown into peristaltic waves, but the sphincters remain contracted. The result is an inflow of impulses to the brain with the resultant sensation of discomfort which constitutes the desire for defecation. The desire can be overcome, as a rule, because the sympathetic center in the cord which controls the sphincters is, by some unknown connection, influenced by the voluntary system. If the desire is not responded to, the rectum relaxes and the stimulation of the nerves ceases and the desire is not again experienced until more material enters the rectum. The act of defecation is initiated by the voluntary contraction of the abdominal muscles, the sphincters then relax and the peristalsis of the colon and rectum is increased, both of which actions are reflexes. When the response to the desire to defecate is repeatedly neglected the rectum loses its sensitiveness and then the initiation of adequate reflexes is interfered with and chronic constipation results.

The more common causes of chronic constipation are: Failure to respond to the desire for defecation; abnormal conditions of the intestine such as frequently follow acute enteritis; the presence of hemorrhoids; lack of tone of the intestinal and abdominal muscles; an insufficient amount of cellulose in the diet; the constant use of irritant cathartics, which accustom the nerve-endings to strong stimulation and thus lessen their sensitiveness to the milder stimulation of food substances.

The best means to prevent and overcome constipation are: To go to the toilet as soon as possible when the desire for defecation is experienced and to have a regular hour for doing so, after breakfast is generally considered the best time; to use a liberal amount of fruit, coarse cereals and vegetables; to take exercises that will call the abdominal muscles into play, and to maintain healthy body tone.

PHYSIOLOGY OF CATHARSIS

With a few exceptions, mentioned later, the **drugs used as cathartics produce their effects** by their local action in the intestine and, as they are not readily absorbed, few of them have much, if any, systemic effects beyond those occasionally induced by their local action. These drugs produce catharsis chiefly either by increasing the amount of material in the intestine or by irritating the intestinal mucous membrane. As will be seen later, those which act by irritation also increase the quantity of fluid in the intestine.

Drugs which act solely by increasing the intestinal contents promote peristalsis in the same manner as food. The increase in the intestinal material may be due chiefly to the presence of the drug itself or to interference with the absorption of water and, in some cases, food.

Drugs which irritate the intestinal membrane induce reflexes which increase peristaltic contractions of the intestinal muscle and thus hurry food residue through the bowel allowing less time for the absorption of water. The irritation of the membrane also increases the amount of blood in the membrane and stimulates the secretion of mucus. Extreme irritation may cause severe congestion and the transudation of fluid from the intestinal blood-vessels.

Cathartics, some more readily than others, are likely to **cause griping pains** or colic, due, it is thought, to the spasmodic contractions of the intestinal muscle induced by the irritation. Either carminatives, described under Volatile Oils, or Belladonna, which lessen spasmodic contractions without interfering with the normal peristaltic contractions, are often given with cathartics that are particularly likely to do this.

The more irritant cathartics are likely to cause **congestion of the pelvic organs,** including, in the female, the uterus. The reason for the congestion of organs not in direct contact with the drugs is unknown.

Classification.—Cathartics which are not irritant, or only mildly so, and only hasten defecation to a slight degree are classed as *laxatives* or *aperients*. Those which are moderately stimulant are termed *purgatives* and those which are decidedly irritant are classed as *drastics*. This classification is not at all arbitrary however, because the mildest laxatives in excessive doses may act as purgatives and large doses of purgatives may have a decidedly drastic effect. Also there is very little difference between the potency of the stronger laxatives and the milder purgatives and their classification by different authorities varies.

Cathartics which produce particularly watery stools, especially the salines, are often referred to as *hydragogues* (from the Greek *hydor* = water and *ago* = to drive). Those which tend to increase the elimination of bile (calomel, castor oil, podophyllum and bile salts) were formerly termed *cholagogues* because they were thought to stimulate the secretion of bile, but it has been found that, with the exception of large doses of bile salts, these drugs do not stimulate the liver to secrete bile, but they, unlike most cathartics, cause forceful contractions of the duodenum and, by doing so, cause contraction also of the bile ducts and the consequent expulsion of the bile stored in the ducts and the gall bladder.

Preparations and dosage:

Laxatives or aperients:

Agar-agar, 1–4ʒ (0.06–15.0).

Euonymus or Wahoo, extract, 1–3 grs. (0.06–0.2 gm.).

Glycerine, 1–2 oz. (30.0–60.0 c.c.).

Leptandra, extract of, 2–5 gm. (0.13–0.3 gm.).

Liquid petroleum or mineral oil, ½–1 oz. (15.0–30.0 c.c.).

Manna, 1–2ʒ (4.0–8.0 c.c.).

Olive oil, 1–3 oz. (30.0–90.0 c.c.).

Sulphur, sublimed, 1–3ʒ (4.0–12.0 gm.).

Tamarind, the preserved fruit is used like other jams.

Purgatives:

Anthracene group.

Aloes, 2–4 grs. (0.13, 0.25 gm.).

Aloes, tincture, ½–2ʒ (0.5–8.0 c.c.).

Aloin (active principle), 1–4 grs. (0.06–0.25 gm.).

There are also a number of pills of aloes combined with other substances, with the exception of the A. B. S. pills the ingredients are indicated by the names of the pills. The A. B. S. pills consist of aloes, belladonna and strychnine.

Cascara sagrada, 15 grs. (1.0 gm.).

extract, 4 grs. (0.25 gm.).

fluidextract, 15.0–60.0 m. (1.0–4.0 c.c.).

aromatic fluid extract, 30–60 m. (2.0–4.0 c.c.).

This contains cascara, glycerin and several aromatic substances.

Regulin, 1–3ʒ (4.0–12.0 gm.). *This consists of cascara and agar-agar.*

Frangula, fluidextract, 15–30 m. (1.0–2.0 c.c.).

Phenolphthalein, 2–3 grs. (0.1–0.2).

Phenolphthalein and agar-agar, 1–3ʒ (4.0–12.0 gm.).

Rhubarb, 15 grs. (1.0 gm.).

Rhubarb extract, 4–8 grs. (0.25–0.5 gm.).

Rhubarb fluidextract, 15 m. (1.0 c.c.).

Rhubarb tincture, (20 per cent.) 1ʒ (4.0 c.c.).

Rhubarb aromatic tincture, 30 m. (2.0 c.c.). *This contains cinnamon, cloves and nutmeg.*

Rhubarb syrup, (10 per cent.) 2 (8.0 c.c.).

Rhubarb compound powder or Gregory's powder, 30 grs. (1.0 gm.). *This contains rhubarb, magnesium and ginger.*

Rhubarb compound pills, 1–5 pills. *Contain rhubarb, myrrh, oil of peppermint.*

Rhubarb Mistura rhei et soda (rhubarb and soda mixture), 1–2 (4.0–8.0 c.c.).

Senna, 1ʒ (4.0 gm.).

Senna confection, 1–2ʒ (4.0–8.0 c.c.). *Contains senna, cassia fistula, tamarind, prune, fig, oil of coriander.*

Senna compound infusion (Black draught), 2 oz. (60.0 c.c.). *Contains senna, fennel and magnesium sulphate.*

Senna fluidextract, 30 m. (2.0 c.c.).

Senna syrup (20 per cent.), 2ʒ (8.0 c.c.).

Mercury group.

Calomel, ½–5 grs. (0.03–0.3 gm.).

Blue mass, 1–5 grs. (0.06–0.3 gm.).

Mercury with chalk or gray powder 5 grs. (0.3 gm.).

Salines:

Carlsbad salt. A mixture of salts, chiefly the chlorid, bicarbonate, and sulphate of sodium and potassium sulphate.

Magnesium citrate, 6–12 oz. (180–360 c.c.).

oxide, 30 grs. (2.0 gm.).

sulphate (Epsom salt), 2–8ʒ (8.0–30.0).

sulphate (effervescent), ½–1 oz. (15.0–30.0 gm.).

Potassium bitartrate (*cream of tartar*), 30–60 grs. (2.0–4.0 gm.).

Potassium citrate, 30 grs. (2.0 gm.).

Potassium citrate (effervescent), 60 grs. (4.0 gm.).

Potassium sulphate, 30 grs. (2.0 gm.).

Rochelle salt (potassium and sodium tartrate) 2–4ʒ (8.0–15.0 gm.).

Seidlitz powder. (*This is prepared in two packages, one, in blue paper, contains Rochelle salt* 2 (8.0 *gm.*) *and sodium bicarbonate; the other, in white paper, contains tartaric acid. For administration, each powder is dissolved in ½ glass of water and one solution poured into the other just before giving it to the patient.*

Sodium citrate, 30 grs. (2.0 gm.).

Sodium phosphate (Glauber's salt), 2ʒ (8.0 gm.).

Sodium phosphate (effervescent), 2–4ʒ (8.0–16.0 gm.).

Lithium citrate (effervescent), 2ʒ (8.0 gm.).

The mineral waters such as Apenta, Carlsbad, Hunyadi, Pluto owe their cathartic properties to some of the above salts. Some of the mineral waters are obtained from springs, but many of them are prepared artificially.

Castor oil (oleum ricini), ½–1 oz. (15.0–30.0 c.c.). (For a young child) 1–3 (4.0–12.0 c.c.).

Castor-lax, 1–2 oz. (30.0–60.0 gm.) (not official). This is a powder made with castor oil and magnesia.

Compound licorice powder (Pulvis glycyrrhizæ), 1ʒ (4.0 gm.). *This contains senna, licorice root, sulphur, fennel and sugar.*

Fel bovis (ox-gall), 5–20 grs. (0.3–1.3 gm.).

Podophyllum, resin of, ⅙ gr. (0.01 gm.).

Drastics:

Colocynth, extract, 2–5 grs. (0.13–0.3 gm.).

compound extract, 4–10 grs. (0.25–0.6 gm.) *contains colocynth, aloes, cardamom, scammony.*

Colocynthin (active principle, not official), 1/10 gr. (1.006 gm.).

Compound cathartic pill, 1–3 pills. *Each pill contains calomel and compound extract of colocynth a.a. 1 gr., resin of jalap 3/10 gr., gamboge ¼ gr.*

Croton oil (oleum tiglii), 1–2 m. (0.02–0.13 c.c.).

Elaterine, 1/10 gr. (0.006 gm.).

triturate, ½ gr. (0.03 gm.).

Euonymus (non-official), 7 grs. (0.45 gm.).

Gamboge, 2 grs. (0.13 gm.).

Jalap, resin of, 2 grs. (0.13 gm.).

compound powder of, 30 grs. (2.0 gm.). *This contains jalap and potassium bitartrate.*

Scammony, resin of, 2 grs. (0.13 gm.).

Vegetable cathartic pill, 1–3 pills. *Each pill contains jalap, podophyllum, leptandra, colocynth, hyoscyamus, oil of peppermint.*

Drugs which act as cathartics by their effects after absorption:

Apocodeine, ½ gr. (0.03 gm.).

Hormonol, ½–1 oz. (15–30 c.c.).

Physostigmine salicylate, 1/60 gr. (0.001 gm.).

Pituitary extract, 15 m. (1.0 c.c.).

Derivation.—With the exceptions mentioned in the text, the cathartics are derived from plants. As knowledge of the names of the plants is not of importance to nurses, space will not be taken to give them.

The drugs which act chiefly by increasing the bulk of the intestinal contents are: agar-agar, glycerine, the mineral oils, the salines and sulphur.

AGAR-AGAR

Agar-agar is a gelatinous-like substance which is derived from various seaweeds. It absorbs water and swells, but it is insoluble in water and it is not absorbed from the intestine. It is usually taken with cereal or mixed with milk or cream. It may be two or three days before a dose has any effect, but if agar-agar is taken regularly, it is likely to cause a soft stool daily so long as its use is continued. There are some objections to its constant use however, viz., (1) it favors the production of putrefactive products in the intestine, both because it provides excellent food material for the intestinal bacteria and because if it is decomposed by bacteria, it yields such products; (2) it tends to prevent the absorption of food; (3) it acts as a demulcent and protects the intestine from irritation by food. To obviate the last objection slightly irritant drugs are sometimes combined with the agar-agar.

GLYCERINE

Glycerine is obtained from fat as a by-product in the making of soap. It acts as a laxative both by increasing the intestinal contents and by a slight irritation of the intestinal mucosa. Both of these effects are due to its power of abstracting water from the tissues.

THE MINERAL OILS

The mineral oils are derived from petroleum. There are a number of brands, known by different trade names, some of which are obtained from Russian and some from American wells. The Russian oils are thicker than the American. These oils are not saponified in the intestine, as are the fixed oils, and they are not absorbed. They act as laxatives by increasing the intestinal contents and by lubricating the intestinal walls. The former action is due to (1) interference with the absorption of water, (2) softening and consequently expanding the food residue, (3) increasing the amount of residue by protecting the

food from the digestive juices and thus retarding its digestion. It is thought that these oils also act as intestinal antiseptics, but this has not been proven. **Objections to their use are:** Their effect on digestion; they are likely to leak from the rectum; they are nauseant to some people. The last objection can be overcome by adding a little lemon or other fruit juice, wine, peppermint or other flavoring extract to the dose.

SULPHUR

Sulphur is an element **obtained** from the vicinity of certain volcanoes. It is distilled by the volcanic heat from sulphur compounds in the depths of the earth and thus the supply is constantly renewed. The sulphur preparation used as a cathartic is a gritty substance that is insoluble in water. **It is best given** in syrup. The compounds which it forms in the intestine are slightly irritating, but its **cathartic action,** which is mild, is due chiefly, it is thought, to increasing the bulk of the intestinal contents.

THE SALINES

The salines are salts that are not readily absorbed from the stomach and intestines. Each salt is formed by the interaction of the salt and alkali indicated by its name. **The effervescent preparations contain,** in addition to the specified cathartic salt, sodium bicarbonate and either or both citric and tartaric acids. These ingredients interact when the salt is dissolved and liberate CO_2. The effervescence which ensues lessens the appreciation of the flavor of the salt and it has a slight, transitory carminative action.

Administration.—An effervescent preparation is not to be diluted until the patient is ready to take it, for the gas escapes quickly. **The dilution of salines is of importance:** Unless otherwise specified, magnesium sulphate is diluted sufficiently to make a 7–8 per cent. solution and the other salts to make about a 5 per cent. solution. The taste of

most saline cathartics is objectionable to the majority of people, but this can be rectified somewhat by diluting the salt in a small amount of hot water (the salts are more soluble in hot than cold water and thus can be dissolved in a smaller amount) and, when cold, adding a carbonated water or lemon juice and a few grains of soda bicarbonate.

Actions and Effects.—As ordinarily diluted (*i.e.*, in the concentrations stated above), **the salines produce catharsis** by increasing the bulk of the intestinal contents and they do this because they prevent the absorption of the water in which they are dissolved, and of the liquid in the intestine, derived from drink and food; also, some investigators consider, by causing the transudation of fluid from the blood-vessels in the intestinal membrane. They do this, it is believed, by precipitating the calcium salts of these tissues. As seen in the section on Calcium, the calcium salts in the tissue of the blood-vessel walls lessen the permeability of the latter and, therefore, if the salts are removed, more fluid will pass through the vessels. Concentrated solutions will, by virtue of their salt action, described page 47, extract fluid from the tissues and blood-vessels of the stomach and intestines, particularly the former and, in this way, promote more or less irritation.

Salines are sometimes given in concentrated solutions when a patient has edema, because a concentrated solution, by extracting water from the intestinal blood-vessels raises the concentration of the blood, whereupon water is absorbed by the blood from the tissues, as described on page 47. Even dilute solutions will have these results to a slight extent because they inhibit the absorption of water taken as beverage and in food. Concentrated solutions should not be given unless prescribed for, as they irritate the stomach, they are more likely to cause nausea than isotonic solutions and they take a longer time to induce catharsis. The reason for the delay of catharsis will be obvious if it is remembered that catharsis depends upon the quantity of water in the intestine and it will of course require some time for a concentrated

solution to extract as much water as is given with a properly diluted dose. On the other hand, if the solutions are so dilute that they are hypotonic to the blood a considerable portion may be absorbed and thus their cathartic effect will be minimized.

Medicinal doses of the salines in the dilutions mentioned on the preceding page will **usually take effect** in about 2 to 4 hours and will, as a rule, induce two or more watery stools without much, if any, griping. They will wash out the entire intestinal tract, though sometimes not very thoroughly. Concentrated solutions may not take effect for 10 or 12 hours and may induce considerable griping. **Excessive doses** of even dilute solutions may cause purging, nausea, tenesmus and, if these results are excessive marked prostration with a rapid weak pulse.

If magnesium sulphate is given in excessive doses enough may be absorbed to depress the central nervous system and produce the effects described on page 114.

Following a dose of a saline cathartic, **the excretion of urine** will be diminished for a time, because of the reduced blood-pressure resulting from the lessened supply of fluid, but though, as previously stated, the cathartic salts are not readily absorbed, they are to some extent and after absorption, by raising the osmotic pressure of the blood they favor the osmosis of liquid from the tissues, as described on page 47, which causes a rise of blood pressure and consequent diuresis.

The amount of a saline solution that will be absorbed will depend (1) upon the concentration of the solution: as a rule, the lower the specific gravity of the solution, the greater the amount absorbed; (2) the concentration of the blood—the greater the concentration of the blood, the larger the amount of solution absorbed, for, it will be remembered, the law of osmosis is that *when two fluids, of unequal concentration are separated by a permeable membrane, the fluid of lesser density will pass more rapidly through the membrane than that of greater density until the fluids are of equal concentration, and the rate of osmosis*

will be in proportion to the differences in density. Conditions that most commonly increase the concentration of the blood are: Restriction of the intake of fluid; unusual loss of water from the body as by hemorrhage, nausea, vomiting, diarrhea, excessive perspiration or diuresis.

When a saline cathartic is given a patient who has edema, the physician should be notified if catharsis does not occur within a reasonable time, because if the solution is absorbed and the kidneys are not functioning properly (which is very likely to be the case when there is edema), the salts may not be excreted and then they will pass into the tissues and by raising the osmotic pressure of the tissue lymph, further the exudation of fluid from the blood and thus increase the edema. This is particularly important in the case of magnesium sulphate, because, if its elimination does not keep pace with its absorption enough may collect in the system to cause the symptoms of poisoning already referred to.

Reduction of the amount of water in the body interferes with **secretion.** This is of particular importance when a woman is nursing her baby, for the supply of milk may be temporarily much lessened following a dose of cathartic salts.

Loss of water also induces intense **thirst** and, unless there is some reason for limiting the supply of liquids, a patient should be given a liberal amount of liquids an hour or so after the cathartic.

THE ANTHRACENE COMPOUNDS

The drugs of the anthracene group are so classified because their active principles are substances that are classified in chemistry as anthracene compounds. Those of plant origin (all those mentioned except phenolphthalein) also contain resinous material that adds to their cathartic value.

Phenolphthalein is a synthetic substance made from

phenol compounds and sulphuric acid. Long before its cathartic properties were known, it was used in laboratories to test the reaction of solutions for it turns pink in the presence of alkalies. It is now also used to test the functioning capacity of the kidneys. For this purpose it is given subcutaneously and, if the kidneys are functioning properly part of a dose will be found in the urine in about 10 minutes and about 60 per cent. will be eliminated within an hour. The presence of the phenolphthalein in the urine is ascertained by adding an alkali to the urine. A small amount of phenolphthalein is excreted through the liver and passes into the intestine in the bile and may have a laxative effect. When the drug is given by mouth only a very small part of a dose is absorbed.

The anthracene compounds, including phenolphthalein, **owe their cathartic properties** to a mild irritation of the intestinal membrane, even in large doses they will not cause harmful inflammation and they do not induce a tolerance to their action, which would necessitate giving increasingly large doses to get effects. For this reason, the drugs of this group, especially phenolphthalein and cascara, are much used in chronic constipation. They will be effectual in from 8 to 12 hours, inducing one or more soft, but not as a rule liquid, stools, with little or no griping. They are best taken at night. Those of vegetable origin contain small amounts of tannin and, therefore, if used in very large doses, their cathartic action may be followed by constipation.

A portion of doses of the anthracene drugs may be absorbed, especially when their use is not followed by free catharsis, and in such case large doses may cause enough depression of the nervous system to give rise to a mild prostration.

Aloes, but not the active principle aloin, tends to cause congestion of the rectum and other pelvic organs and therefore should not be taken by those who have hemorrhoids nor during menstruation, unless prescribed to relieve amenorrhea.

Rhubarb contains a bitter principle as well as its anthracene compounds and is therefore often used to aid digestion.

Senna and **frangula**, especially the latter, are more irritant and thus more apt to cause griping pains than the other drugs of this group.

MERCURY COMPOUNDS

The derivation and nature of the mercury compounds are given under Mercury and thus only their cathartic action need be discussed here.

Calomel is a non-irritating powder, but as soon as it enters the duodenum it interacts with alkaline salts there present and is changed to mercurial salts that are irritant and thus promote peristalsis. The intensified contractions of the duodenum induced by the calomel promotes contraction of the **bile ducts** and thus cause the expulsion of the bile stored in the ducts and gall-bladder. Calomel, however, does not stimulate the **colon** to such an extent as the small intestine and, consequently, a small dose may not be effectual, while a large one is likely to cause intense griping and, when the calomel does not produce adequate catharsis, headache, nausea and sometimes vomiting are likely to ensue. For these reasons, a dose of calomel is generally followed, in about six hours, by a dose of salts and the calomel is sometimes given in divided doses, *i.e.*, a small dose (⅛ or ¼ grain) is given at intervals of about fifteen minutes until the desired amount has been administered. Sodium bicarbonate is very commonly given with calomel. Formerly, the intention of this was to prevent the hydrochloric acid of the gastric juice changing the calomel to bichlorid of mercury, but it has been demonstrated that this is not at all likely to occur and that sodium bicarbonate, in the amounts in which it is used, could not prevent the reaction. However, the carminative action of the CO_2, which is liberated when the soda interacts with the acid gastric juice, helps

to overcome any tendency to nausea. Albuminous foods, such as milk and eggs, should not be given soon after a dose of calomel, for the albuminate of mercury which may be formed is not irritant.

As calomel tends to hasten the elimination of bile and when followed by a dose of salts, the combination causes a thorough purge of the entire intestinal tract, it is very commonly used when a patient is jaundiced or bilious.

Blue mass and gray powder, especially the latter, are less irritant than calomel and the gray powder is very commonly used for children.

CASTOR OIL

Castor oil is, like other fixed oils, an ester of glycerine and a fatty acid, the fatty acid being *ricinoleic acid.* The oil is split to these constituents in the intestines and the fatty acid is saponified, yielding thereby a *ricinoleate soap.* This soap is very much more irritant than the soaps formed by food fats and it is not, as they are, easily absorbed, thus it acts as an irritant on the entire intestinal tract, inducing, in moderate doses, several soft and sometimes watery movements in from 3 to 6 hours. It does not, as a rule, unless taken in large doses, cause much griping, but it does induce congestion of the female pelvic organs and therefore should not be taken, unless prescribed by a physician, during menstruation or pregnancy. By its action on the duodenum, it increases the elimination of bile. It causes such a thorough catharsis of the entire intestine that its use is likely to be followed by constipation for a day or two.

Though sodium ricinoleate is not readily absorbed, enough may be taken up by the blood and excreted through the mammary glands to act as a cathartic for a nursing infant. The ricinoleate is also excreted in the urine.

Castor oil is a particularly valuable cathartic when it is necessary to rid the intestine of irritating material that is causing diarrhea both because of the thorough purge which

it induces and its tendency to promote subsequent constipation.

Objections to the use of castor oil are its nauseant taste and its tendency to coat the tongue and mucous membrane of the mouth and throat and thus prolong this sensation. **To overcome these objections** a dose must be properly prepared. A good method is to rinse a small glass with lemon or orange juice, leaving the juice in the glass; add a small piece of ice (it should be the size of a pea when the dose is given to the patient); add the oil, pouring it directly on the ice; add more juice and, just before handing the glass to the patient, some carbonated water. Have a glass of lemonade at hand to give the patient as soon as the dose is taken. Holding a small piece of ice in the mouth for a short time before taking oil will tend to lessen the appreciation of the obnoxious flavor because cold, being a protoplasmic depressant, lessens the sensitiveness of the taste-buds.

Castor oil should never be given children in milk for it is likely to make them conceive a distaste for a valuable food.

OLIVE OIL

If olive oil is taken in amounts (at least 1 ounce) that add considerably to the quantity of fat taken as food the soap into which it, like all fats, is transformed in the intestine, may not all be absorbed and will then act as a laxative. Olive oil has been extensively used as a rectal injection to soften feces, but it has been found that it does not do this as well as water.

COMPOUND LICORICE POWDER
(PULVUS GLYCYRRHIZÆ)

Compound licorice powder **owes its cathartic properties** chiefly to its sulphur and senna, the glucoside glycyrrhizin (the active principle of the licorice) is only slightly laxative

and the chief purpose of the fennel (which is a volatile oil) is to improve the flavor and prevent griping. **The powder acts** upon the small, as well as the large, intestine. If taken while the stomach is fairly empty it will produce liquid stools in about 3 to 6 hours, but if the dose becomes mixed with food in the stomach, it will take longer to produce effects. As a rule, unless taken in large doses, compound licorice powder does not cause griping. It is frequently prescribed for patients who have hemorrhoids because it does not cause much congestion of the intestine and, as the stools are liquid, the hemorrhoids are not irritated during defecation.

For administration, the powder should be mixed with just enough water to make it easy to drink, but a glass of water must be at hand to give the patient as soon as the dose is taken. It is best taken at night.

FEL BOVIS OR OX-GALL OR BILE SALTS

Fel bovis is prepared from dried bile obtained from the ox. It owes its cathartic properties to bile salts. These are slightly irritant to the mucous membrane of the intestine. A considerable portion of a dose may be absorbed and this is excreted through the liver and tends to stimulate the secretion of bile.

PODOPHYLLUM

The composition of podophyllum resembles that of the drastics, but it is less irritant than the latter and is therefore usually classified with the purgatives. It requires about 8 hours to produce catharsis.

DRASTICS

With the exception of croton oil, the **drastic cathartics owe their cathartic effects** to resinous glucosides and acids. They are, except in large doses, only slightly irritant to the stomach and duodenum, but after they

become mixed with the bile, their irritant action is greatly increased and, even in moderate doses, they will induce several profuse, watery stools in from 2 to 4 hours. **They are likely to cause** considerable griping and congestion of the intestinal wall and pelvic organs. They affect the entire intestinal tract and thus will cause a thorough purge. Large doses, or even moderate doses, if they are not eliminated, are likely to cause inflammation of the intestine and, though they are not readily absorbed, enough may be taken up under such circumstances to irritate the **kidneys.** For this reason, if effectual catharsis does not occur in about 4 hours a saline cathartic or an enema is generally prescribed.

Poisonous doses will induce nausea, vomiting, purging and collapse. As these symptoms are due almost entirely to the local effects, the **treatment** is directed to correcting these and consists in giving a saline cathartic and enemata of first normal salt solution and then a lubricant, as olive oil. Fluid is also given liberally, by mouth if possible, and, if not, by enteroclysis. It is needed to replace that lost by the purging and vomiting and to lessen the irritation of the kidneys.

Drastic cathartics should not be used by a person who has hemorrhoids or inflammation or ulcers of the gastro-intestinal tract; neither should they be taken during menstruation nor pregnancy, for they may cause hemorrhage and, in the latter case abortion unless the need is urgent, they should not be given the aged nor those in a debilitated condition for their use is then likely to cause extreme depression.

Croton oil (*oleum tigli*) **is used** more especially for unconscious patients, when immediate catharsis is essential, because such a small amount of oil is necessary that it is easily administered. It is usually given on sugar or a few drops of melted butter or olive oil which, if the patient is not conscious, is dropped on the back of the tongue.

Croton oil owes its drastic properties to an extremely irritant acid—crotonic acid.

SUPPOSITORIES

Irritation in the rectum produces reflexes that induce peristalsis in the colon and, therefore, suppositories of substances such as glycerine and soap will, if inserted in the rectum, cause catharsis.

CATHARTIC ENEMATA

Cathartic enemata are used, as a rule, when immediate catharsis is required and when for any reason a cathartic cannot be taken by mouth. As their nature and methods of administration are described in all text-books of nursing procedures, space will not be taken to do so here.

CATHARTICS WHICH ACT AFTER ABSORPTION

With the exception of hormonol these drugs are all discussed elsewhere and thus only the means by which they promote catharsis will be mentioned.

Hormonol is a liquid prepared from the spleen of a rabbit. Its active principle is thought to be a hormone (*i.e.*, a chemic substance made by a gland that, after absorption, stimulates other organs). Hormonol is occasionally used to overcome post-operative tympanites or constipation. It is given intravenously or intramuscularly. It acts as a cathartic by stimulating the intestinal muscle tissue. For unknown reasons it occasionally causes collapse, thus patients receiving it must be carefully watched.

Apocodeine increases peristalsis by depressing the sympathetic (inhibitory) nerve-endings in the intestinal muscle, thus allowing the impulses coming over the vagus (motor) nerve-fibers free action.

Physostigmine (eserine) stimulates the vagus nerve-endings in the intestinal muscle, thus furthering its contractions.

Pituitrin, like hormonol, stimulates the muscle tissue of the intestine.

SYNOPSIS OF DATA REGARDING CATHARTICS THAT ARE PARTICULARLY IMPORTANT FOR NURSES TO REMEMBER

1. Time usually required to produce effects:			2. Cathartics that promote the elimination of bile:	3. Cathartics that promote thorough purging:
Less than 4 hours	4–8 hours	8–12 hours		
Drastics Physostigmine Isotonic solutions of salines	Castor oil Mercury cathartics	Agar-agar Anthracene cathartics Licorice powder Mineral oils Olive oil Podophyllum Salines in concentrated solutions Sulphur	Castor oil Mercury cathartics Podophyllum	Castor oil Calomel followed by salts Drastics
			4. Cathartics that promote congestion of the pelvic organs:	5. Cathartics that lessen the secretion of milk:
			Aloes Castor oil Drastics	Drastics Salines

VOLATILE OILS. STEAROPTENS. SPICES AND DRUGS WHICH OWE THEIR PROPERTIES TO SUCH COMPOUNDS. COUNTERIRRITANTS

Volatile or ethereal oils are volatile, and usually aromatic, substances to which fruit and many spices and other plant substances owe their odor and flavor.. Some of the spices and drugs classed under this heading owe their properties to resinous compounds, but the actions of these are so similar to those of the volatile oils that they need not be considered separately.

In spite of their name, the volatile oils have very little in common with the fixed oils. **They consist** chiefly of mixtures of the hydrocarbons known in chemistry as *terpenes*, holding in solution substances, usually solids, termed *stearoptens*.

The stearoptens can be separated from the oils by volatilizing the latter at a low temperature. Some of these substances belong to the same chemical group as carbolic acid, *i.e.*, the *phenols*.

Some volatile oils exist as such in plants and can be readily extracted by pressure or distillation, others are only developed by special treatment. For example, the oil in mustard is evolved from certain constituents of the latter when it is mixed with water, by the action of a ferment, also a constituent of the mustard. An important thing to remember in regard to this ferment is that it is destroyed by a high temperature about 140°F. (60°C.) and it is rendered inert at an even lower temperature. If the ferment is inactive, the oil, and, consequently, the flavor and irritant properties of the mustard, will not be developed.

The oils exist in different parts of plants, for example, camphor is obtained from the wood of certain species of

trees; while some others are obtained from the gum or sap of trees, some from the leaves; some from the fruit, etc.

Nature of Preparations.—For therapeutic purposes, the extracted oil or stearopten may be used or, dilutions of these, as spirits and waters; or as in the case of asafetida, mustard, and the spices, what is almost the crude drug may be employed or, when the active principle is a resin, fluidextracts or tinctures made from the crude substances.

Certain volatile oils and their stearoptens contain other compounds which give them important special qualities and these are classified with drugs having similar properties. Important examples are, the oils of birch and wintergreen and their stearopten, methyl salicylate, which have salicylic acid actions, as well as those characteristic of volatile oils.

Preparations and Dosage.—A number of preparations belonging to this group are now so seldom used except certain of them (anise, almond, orange, etc.), as flavors, that it is not necessary to list them. It will be sufficient to remember that the average dose of the more irritant oils, such as **pennyroyal, rue, sage, and tansy,** is 1–3 m. (0.06–0.2 c.c.), of less irritant ones, as **peppermint and fennel,** 5 m. (0.3 c.c.); of spirits, 15 m.–1 ʒ (1.0–4.0 c.c.) of waters 1–2 ʒ (4.0–8.0 c.c.).

Aromatic powder, 10–30 grs. (0.6–1.0 c.c.). *This contains cinnamon, cardamom, ginger and nutmeg.*

Asafetida, tincture of, 15–30 m. (1.0–2.0 c.c.).

emulsion of, ½–1 oz. (15.0–30.0 c.c.).

pills of, 1–3. *Each pill contains* 3 *grs. of asafetida.*

Apinol oil, 5–15 m. (0.3–1.0 c.c.). *Similar to oils of pine and eucalyptus.*

Apiol, 3–10 grs. (0.2–0.6 gm.). *The stearopten of the oil of parsley.*

Apioline, 3–10 grs. (0.2–0.6 gm.). *Obtained from apiol.*

Buchu, fluidextract, ½–1 ʒ (2.0–4.0 c.c.).

Cajuput, oil of, 5–15 m. (0.3–1.0 c.c.).

Camphor, the stearopten, 3–10 grs. (0.3–0.6 gm.).

oil of, 5–10 m. (0.3–0.6 c.c.).

spirits of, 15–30 m. (1.0–2.0 c.c.).
water of, 15 m.–1ʒ (1.0–4.0 c.c.).

Camphorated oil, 30 m.–3½ʒ (2.0–15.0 c.c.). This contains 20 per cent. of the stearopten in either cotton-seed or olive oils. It is the preparation most commonly used.

Monobromated camphor, 5–15 grs. (0.3–1.0 gm.).

Capsicum, tincture, 30–m..1ʒ (2.0–4.0 c.c.).

Cardamom, tincture, ½–1ʒ (2.0–4.0 c.c.).
compound tincture, 1–2ʒ (4.0–8.0 c.c.).

Chenopodium, oil of, 3–5 m. (0.2–0.3 c.c.)

Cinnamon, oil of, 1–3 m. (0.06–0.2 c.c.). For a tooth cavity, 1 drop on cotton.

Cloves (*cardophylus*), oil of, 1–3 m. (0.06–0.2 c.c.). For a tooth cavity, 1 drop on cotton.

Copaiba, oil of, 5–30 m. (0.6–2.0 c.c.).

Cubebs, oil of, 5–15 m. (0.3–1.0 c.c.).
fluidextract, 10–30 m. (0.6–2.0 c.c.).
oleoresin of, 10–15 m. (0.6–1.0 c.c.).

Erigeron, oil of, 5–30 m. (0.3–2.0 c.c.).

Eucalyptus, oil of, 5–15 m. (0.3–1.0 c.c.).

Eucalyptol, 5–15 m. (0.3–1.0 c.c.). *Obtained from eucalyptus.*

Eugenol, 1–3 m. (0.06–0.2 c.c.). *Stearopten of oil of cloves.*

Ginger, tincture, ½–1ʒ (2.0–4.0 c.c.).

Juniper, oil of, 5–15 m. (0.3–1.0 c.c.).

Menthol, 1 gr. (0.06 gm.). *Stearopten of oil of peppermint.*

Mustard (*sinapis*), 1–2ʒ (4.0–8.0 gm.) in tepid water as emetic.

Pine, oil of, 1–5 m. (0.06–0.3 c.c.).

Sandalwood, oil of, 5–15 m. (0.3–1.0 c.c.).

Terebin, 5–30 m. (0.3–2.0 c.c.). *Prepared from oil of turpentine.*

Terpin hydrate, 1–5 grs. (0.06–0.3 gm.). *Prepared from oil of turpentine.*

Thymol, 1–50 grs. (0.06–3.3 gm.). *The stearopten of oil of thyme. Large doses are used only as anthelmintics and*

with the precautions mentioned in the section describing the use of the drug as an anthelmintic.

Tar, oil of, 1–5 m. (0.06–0.3 c.c.).
syrup of, 1–2ʒ (4.0–8.0 c.c.).
ointment, for external use.

Uva-ursi, fluidextract, 5–15 m. (0.3–1.0 c.c.).

Valerian, fluidextract of, 30 m. (2.0 c.c.).
tincture of, 1–2ʒ (4.0–8.0 c.c.).
ammoniated tincture of, 1–2ʒ (4.0–.80 c.c.).

New Non-official Preparations.

Borneol valerate 5–10 m. (0.3–0.6).

Validol or menthol valerate, 5–15 m. (1.0 c.c.). *A compound of menthol and valevianic acid which is obtained from valerian.*

Validol camphorate, 5–15 m. (p, 3–1.0 c.c.).

Fate in the Body.—The oils and stearoptens mentioned in this section are not absorbed through the skin, though they may penetrate the outer layers sufficiently to reach the superficial nerve-endings and blood-vessels. The oils are readily absorbed from the stomach and intestines. The stearoptens are absorbed, if they are dissolved in oil or alcohol, but not to any extent when in their natural state, for they are only very slightly soluble in water and the digestive juices and this, of course, interferes with their absorption. After absorption, these substances are oxidized to simpler compounds and the latter are excreted, chiefly in the urine, but also through the respiratory tract and sometimes in the sweat. Some of the products of oxidation are aromatic and impart an odor to the urine or breath, this, in many cases is quite different from that of the original compound; for example, the products of turpentine oxidation give an odor of violets to the urine.

Actions.—The drugs of this group are protoplasmic irritants, but with a few exceptions they do not, except in excessive doses, cause inflammation or destruction of human tissue. Their effects, however, are more marked on lower forms of life, as bacteria. Like most irritants, they are weakened by dilution and thus few of them, unless

taken in excessive amounts, act upon the tissues after absorption. Certain of them, however, irritate the organs through which they are excreted; in poisonous doses they tend to first stimulate and then depress the central nervous system.

Effects and Uses.—There are some slight differences in the effects produced by the various drugs of this group, but they are due chiefly to different degrees of potency and to the tissues upon which they act most strongly. These slight differences, however, make certain ones more suitable for some purposes than others, but, in many cases, it is not so much difference in the action of a drug that has determined its use as its cost or some physical property, as its flavor or degree of solubility.

Effects common to all the drugs of this group with some slight variations are as follows:

1. **They are antiseptic,** certain of them strongly so, but as they are not readily soluble in water, they are not of much use in surgery. However, the antiseptic properties of a number of them are made use of for special purposes; viz.:

(*a*) To preserve food—expecially the spices.

(*b*) In dentistry, to, especially, disinfect cavities in the teeth—the oils of cinnamon and cloves and the stearopten eugenol.

(*c*) For the nasal cavities, mouth and throat—especially the oil of eucalyptus, and the stearoptens camphor, menthol and thymol.

(*d*) For the intestines—thymol and it is possible that all those used as carminatives may have a strong enough antiseptic action, in therapeutic doses, to inhibit the activity of bacteria to some extent.

(*e*) For the urinary tract—especially the oils of cubebs, copaiba and sandalwood.

(*f*) In chronic skin diseases—oils of cade and tar.

(*g*) As a specific for the pneumococcus—camphor.

Certain ones, especially, chenopodium, thymol and turpentine also destroy worms, *i.e.*, they are **anthelmintics.**

2. When concentrated preparations of most of these drugs are kept in contact with the **skin** they induce varying degrees of irritation with consequent dilation of the superficial blood-vessels. As the result of this, there is an increased amount of blood in the area, which makes the part warm and red. **Sensory nerve-endings** are stimulated and this gives rise to sensations of tingling and smarting and, if pronounced, will have counterirritant effects as described on page 285. The drugs of this group most commonly used as counterirritants are camphor, capsicum, mustard and turpentine.

Certain members of the group, especially camphor, menthol and the oils of apinol, cloves and cinnamon, after stimulating sensory **nerve-endings,** depress them to some extent and thus the tingling and smarting that they induce is followed by numbness and partial anesthesia. Peppermint and menthol stimulate the cold spots in the skin and thus give rise to a sensation of cold, even when the skin is unusually warm.

3. All the drugs of this group stimulate **olfactory nerve-endings** and, some of them, the **taste-buds,** thereby inducing sensations of flavors that, with a few exceptions, are pleasant to most people. This stimulation also promotes reflexes that increase the secretion of saliva and gastric juice and it tends to stimulate the appetite. This action of volatile oils and spices, which, in addition to producing the physiological effects just mentioned, causes them to make food savory and to overcome the obnoxious flavors of some drugs, furnishes the common reason for the use of the majority of the substances under discussion. Of course, when used solely for this purpose, they are employed in relatively small amounts.

Asafetida and valerian have a strong unpleasant flavor which, it is thought, is chiefly responsible for the psychic stimulation that helps to overcome hysteria.

4. These substances affect **mucous membrane** in about the same way as the skin, but more readily, also they increase the secretion of mucus and, if kept in contact

with a part, they may possibly stimulate the membrane cells, which action, with the effect upon the blood-vessels and the antiseptic action of the drug, is of value in overcoming inflammatory conditions, such as exist in the throat and nose in pharyngitis and rhinitis. Eucalyptus, thymol, menthol and pine, are the drugs most commonly used for this purpose and they are generally employed either in ointment, or in oil that is sprayed upon the part, or they are inhaled.

5. **In the stomach and intestines** the conditions produced by moderate irritation of the lining membrane, induce a sensation of warmth and well-being and help to overcome nausea and to induce the expulsion of gas, *i.e.*, they have a carminative action. Different reasons are given for the expulsion of gas, some investigators believe that it is due to increased peristalsis, induced by the irritation, but others think that it is the result of relaxation of the muscle tissue of the stomach and intestines, which overcomes the spasmodic contractions of the sphincters. Some of these drugs certainly do prevent the spasmodic contractions (griping) produced by irritant cathartics. The antiseptic action of these drugs may also be of some slight value in overcoming flatulence. Those chiefly used as carminatives, when given by mouth, are cardamom, capsicum, ginger and other spices. Asafetida and turpentine are often added to soap enemata, to increase their irritant action and thus help in the expulsion of gas, and turpentine is applied externally to the abdomen to do so in the manner explained under counterirritants.

Some of the more irritant drugs of this group,—*e.g.*, apiol, apioline, pennyroyal, ginger, rue, sage and tansy—by effects not well understood, produce pronounced hyperemia of the **pelvic organs**, including the **uterus** and therefore they have been used as emmenagogues but the four last mentioned are rarely employed at present, because they, unlike most of the group, tend to produce severe inflammation in even moderate doses. They are often used to produce criminal abortion. They may do

so on account of the congestion which they promote in the uterus, but death, as the result of irritation of the alimentary canal and kidneys, has occurred without abortion taking place.

7. **Still another effect in the alimentary canal,** is the stimulation of receptors and, consequently, in large doses, the drugs of this group will produce reflex stimulation of nerve-centers and this may help a person to overcome hysterical tendencies; valerian is especially likely to do so.

8. In excessive doses, all these substances, like other irritants, will irritate the **organs through which they are eliminated,** but a few of them do so in moderate doses and these are sometimes used to increase the activity of the organs they affect. Those which influence the kidneys sufficiently to be of value as diuretics are: Oil of juniper, the fluidextracts of buchu and uva-ursi and the urinary antiseptics mentioned on page 278. Those which affect the bronchial membrane sufficiently to act as expectorants are the oils of apinol, camphor, copaiba, eucalyptus, pine, tar, and the turpentine derivatives terpin hydrate and terebene. At one time it was thought that these expectorants would also act as antiseptics in the respiratory tract during their elimination, but it is now believed that they are not excreted through the bronchial membrane in sufficient quantity to do so to any extent.

With the exception of camphor, these drugs, in the small amounts in which they are used as flavors and in therapeutics, have practically **no effects after absorption,** but, if taken in excessive quantities, they will first stimulate and then depress, the nervous system and sometimes the heart muscle.

The stearopten camphor dissolved in oil, can be used in large enough amounts to stimulate the central nervous system without inducing subsequent depression. Its stimulant action is most marked on the **medullary centers** and it is thought that it may also stimulate the **heart muscle.** For some unknown reasons, camphor causes

dilation of the superficial **blood-vessels**, but, because of the stimulation of the vasoconstrictor center, contraction of other vessels, except those of the brain, lungs and heart, which are not supplied with vasoconstrictor nerves. As the result of these actions, **blood pressure** is raised and the circulation improved. **The pulse** becomes stronger, but its rate varies, it may remain unchanged or become either faster or slower. Because of the dilation of the vessels on which the pulsation is felt, the pulse has a bounding character. As the respiratory center is stimulated, **breathing** is deepened and facilitated.

Also, camphor tends to increase the secretion of **sweat**, probably as the result of the increased pressure in the blood-vessels around the sweat glands and, in maximum therapeutic doses, it inhibits the activity of the **pneumococcus**, an organism that causes lobar pneumonia.

Thus camphor is used: (1) In liniments, as a counter-irritant; in local applications to the throat and nasal cavities, as an antiseptic stimulant of the mucous membrane; (2) as a carminative; (3) to stimulate the circulation; (4) as a specific in pneumonia.

For the two purposes last mentioned it is, as previously stated, the stearopten dissolved in oil that is used and it is **administered** by hypodermic injection, both to get quicker results and because the large doses used for these purposes are likely to cause nausea and vomiting, if they are given by mouth.

Summary of the chief uses of the volatile oils, etc. that are most commonly employed for therapeutic purposes:

Asafetida is used as a carminative and an antihysteric.

Apinol is employed as an anodyne and antiseptic on burns and the like, and as an expectorant.

Camphor, see above.

Capsicum is used for the same purposes as the spices.

Cardamom is employed as a flavoring substance for drugs with an unpleasant taste; to aid digestion; and as a carminative.

Chenopodium is used as an anthelmintic.

Cinnamon, oil of, is used as an analgesic antiseptic in dentistry; as a flavoring substance; as a carminative; it is combined with irritant cathartics to prevent griping.

Cloves, oil of, is used for the same purposes as oil of cinnamon.

Copaiba is used as a diuretic and urinary antiseptic; as an expectorant; and it has a slight laxative action.

Eucalyptus is used chiefly as an antiseptic and local stimulant for mucous membranes, especially those of the nose and throat; and as an expectorant. For use on the mucous membranes it is employed as an ingredient of lozenges, and in oil solutions and ointments, or it is added to boiling water and the vapor inhaled. For internal use it is generally given in capsules, or in oil, or on sugar. Like most volatile oils, it is only very sparingly soluble in water.

Fennel is combined with irritant cathartics to avoid griping.

Ginger is very commonly used as a carminative and to overcome uterine colic during menstruation. For these purposes it is generally used as a tincture or combined with other spices.

Juniper is used as a diuretic.

Menthol is used in solid form, as a cooling counterirritant, for the relief of headache and neuralgia. In an oil solution or in petroleum or as an ointment, it is used as an antipruritic (to allay itching) and as an antiseptic and local stimulant for inflamed mucous membranes, especially those of the nose and throat; and the vapor, which passes readily from the crystals, is inhaled to obtain relief in rhinitis. It is occasionally taken by mouth, for carminative action.

Mustard is used chiefly as a counterirritant and an emetic.

Peppermint is used as a flavor and a mild carminative.

Pine oil is used for the same purposes as eucalyptus.

Sandalwood is employed as a urinary antiseptic.

Spices are occasionally used as counterirritants, but they are more commonly employed to stimulate the gastric juice (in food), and as carminatives and emmenagogues. For the two purposes last mentioned, various combinations of the spices are often used, as the aromatic powder; and they are also taken in liquid preparations containing other carminatives, such as alcohol, ether, and ammonia.

Tar preparations are used externally, as antiseptic tissue stimulants, in the treatment of parasitic skin diseases, and, internally, as expectorants.

Terebene and terpin hydrate are used chiefly as expectorants.

Thymol is used chiefly as an antiseptic mouth wash; an intestinal antiseptic and an anthelmintic. For internal use it is generally given in capsules, it must not be given in oil or alcohol if used in more than minute amounts, because it is freely soluble in these liquids and a toxic quantity may be absorbed. Thymol is one of the most poisonous drugs belonging to this group, its poisonous effects being due chiefly to depression of the nervous system and heart.

Turpentine is used chiefly as a counterirritant, and chiefly in enemata, as a carminative; it is occasionally used as an expectorant, but its derivatives, terebene and terpin hydrate, are more commonly employed for this purpose.

Valerian is employed as an antihysteric.

Toxicology.—The symptoms of poisoning depend upon the excessive irritation of the alimentary tract and the kidneys and the excessive stimulation of nerve-centers (both from the reflexes and the action of the drug after absorption) followed by depression. Thus the usual ones are: Nausea, vomiting, diarrhea with, sometimes, blood in the vomitus and stools; convulsions, delirium followed by unconsciousness and collapse. The treatment for poisoning is that described on pages 68 and 69.

Constant use of excessive amounts of any of these irritants is likely to produce a chronic gastritis.

COUNTERIRRITANTS

Counterirritants are, as previously stated, agents that, by irritating the skin, counter or relieve irritation that already exists. To be of value as a counterirritant, a drug must be able to promote a very decided degree of irritation without injuring the tissue. Nearly all substances which do so are of a volatile nature.

Counterirritants are classified, according to the degree of irritation which they are generally used to promote, as rubefacients and vesicants.

As their names imply, **rubefacients are** those used to produce reddening and **vesicants** those employed to induce blisters. The reddening is the result of an increased amount of blood in the skin, as the result of dilation of the blood-vessels by the irritation As previously stated, it is not known positively how irritation causes the dilation. In addition to this effect, sensory nerve-endings are stimulated and, it is believed, the impulses arising from this stimulus stimulate centers in the cord which promote the contraction of blood-vessels in the tissues and viscera situated beneath the irritated areas of skin,[1] and thus relieve congestion (a common cause of pain) in these parts. Also, centers which cause contraction of muscle tissue beneath the irritated areas may be stimulated; it is in this way that hot stupes applied to the abdomen relieve flatulence. Counterirritants also relieve pain, it is believed, (1) because the impulses they start, while passing up the cord, modify those passing from the irritated organs; and (2) by psychic influence or suggestion.

The rubefacients in common use are: Heat, various members of the volatile oil group, but especially those mentioned on page 279, ammonia, antiphlogistine or clay poultice, chloroform, iodine, methyl salicylate and guaiacol —these are all described elsewhere. Drugs used for this

[1] As previously stated, in the spinal cord, afferent neurones from any portion of skin form synapses with efferent neurones that innervate the tissues and viscera lying beneath that area.

purpose are generally incorporated in liniments, pastes, plasters and poultices. As the method of preparing and using these are described in all text-books of nursing procedures, space will not be taken to do so here.

The only vesicant in common use is cantharides or Spanish fly. This is prepared from the crushed body of a beetle known as the *Cantharis vesicatoria*, and it is employed chiefly incorporated in plasters or mixed with collodion (for methods of using these preparations, see a text-book of nursing procedure).

Formerly, a tincture of cantharides was employed as a diuretic, but its use has been almost abandoned, because the drug is very irritating to mucous membranes and the **kidneys.** Nephritis has been caused even by the amount of cantharides absorbed from external applications. For this reason **the size of a plaster,** or other application, must not exceed 3 inches and, as a rule, the size prescribed is ½–1 inch.

The value of cantharides as a vesicant is that, as it is not as irritant to the skin as most of the substances used as counterirritants, it acts slowly and thus the effects of a moderate degree of irritation can be maintained for several hours; also the blister induced, if care is taken to avoid infection, heals readily and without producing scar tissue, which is not always the case with the blisters caused by heat and irritants which cause vesication quickly.

The reason that irritation causes a blister or vesicle is that, as the result of the increased amount of blood in the irritated part, there is excessive transudation of fluid from the vessels into the skin and this separates the epidermis from the derma.

ANTHELMINTICS, VERMICIDES AND VERMIFUGES

Anthelmintics are agents used to destroy or remove worms infesting the intestines. **The species of worms** with which humans most frequently become infected are: Pin- or thread-worms (*oxyuris vermicularis*); round-worms (*ascaris lumbricoides*); tape-worms (*tenia*); hookworms (*uncinaria* or *ankylostoma duodenale*). Infection takes place as the result of eating food containing the eggs of the worms and hookworms also enter the body through abrasions in the skin after which they are carried to the intestines by the blood.

Anthelmintics are commonly classed as vermicides—those which kill the worms—and vermifuges—those which merely affect their removal. They are also classified according to the worms upon which they act most readily as: *Lumbricides*, and *lumbrifuges*, those which act on round-worms, viz., chenopodium, santonin and spigelia; *teniacides* and *teniafuges*, those acting on tape-worm, viz., aspidium (male-fern); amorphous filicic acid; cusso; granatum (pomegranate); kamala; pepo (pumpkin-seed); turpentine.

Anthelmintics most commonly used for hook-worm are: Aspidium, chenopodium and thymol.

The small pin-worms, which may be present in the colon in great abundance, do not, as a rule, cling to the intestinal wall and thus they can sometimes be removed by thorough catharsis or colon irrigation. If these means are not effectual an enema containing one or other of the following substances is given: Alum, lime-water, normal salt solution, quassia, tannic acid, vinegar.

Preparations and dosage of anthelmintics:

Alum, 30 grs. (2 gm.) to 1 pint (500 c.c.) of water, as a colon irrigation.

Aspidium (*male-fern*) oleoresin of, 1–2ʒ (4.0–8.0 c.c.).

Amorphous filicic acid, 10 grs. (0.6 gm.). *An extract of aspidium.*

Chenopodium, oil of, 5–45 m. (0.3–3.0 c.c.).

Cusso, powdered flowers of, ½ oz. (15.0 gm.).

Cusso, fluidextract of, 1–4ʒ (4.0–16.0 c.c.).

Kamala, 1–2ʒ (4.0–8.0 c.c.).

Lime-water, 1–2 pts. (500–1000 c.c.) as a colon irrigation.

Pomegranate (*granatum*) fluidextract of, 30 m. (2.0 c.c.).

Pelletierine tannate, 4 grs. (0.25 gm.). *A tannate of the alkaloid of pomegranate.*

Pumpkin-seed (pepo), 2–4 oz. (60–120 gms.).

Pumpkin-seed, oil of, ½ oz. (15.0 c.c.).

Quassia, infusion of, 10 per cent., as a colon irrigation.

Santonin (*wormseed*), ½–2 grs. (0.03–0.13 gm.).

Spigelia (*pink-root*) fluidextract of, 1–2 (4.0–8.0 c.c.).

Tannin, 30 grs. (2 gm.) to 1 pt. (500 c.c.) of water, as a colon irrigation.

Thymol, 5–15 grs. (0.3–1.0 gm.) in divided doses.

Turpentine, oil of, ½–1 oz. (15.0–30.0 c.c.).

Administration.—It is customary before giving an anthelmintic to limit the diet for 24 hours and to give a purgative 6 or 8 hours previous to the administration of the anthelmintic. This treatment is intended to rid the intestine of material that would protect the worms from the anthelmintic. In order to avoid irritating the stomach and causing nausea, most anthelmintics are given in capsules or by special methods mentioned later. Unless the anthelmintic itself causes profuse catharsis, a quickly acting cathartic, usually a saline, is given about 2 hours after the anthelmintic.

Fate in the Body.—The only drugs used as vermicides that are not described elsewhere are certain very poisonous ones that are not readily absorbed and thus, normally, almost the entire dose is excreted in the feces.

Actions and Effects.—Some of the **vermifuges** (alum, lime-water, sodium chloride and tannin) owe their effects to their astringent action. This causes shrinking of the

protoplasm of the worms (which lessens their vitality) and of the intestinal membrane (which widens the lumen of the bowel) and thus facilitates washing out the parasite. The other vermifuges (pepo, quassia, and small doses of the vermicides) produce an irritation that results in the withdrawal of the worms from the vicinity of the poison.

The vermicides are irritant poisons and, in addition to stupifying or killing the worms, they will cause more or less irritation of the alimentary canal and thereby produce conditions similar to those induced by the volatile oils, described on page 284. Apart from this they normally have no marked effect. If, however, their elimination is delayed, a sufficient amount may be absorbed to induce the poisonous effects mentioned in paragraphs following.

It is most important that free catharsis follow the use of an anthelmintic, both to rid the intestine of the worms and the anthelmintic.

ASPIDIUM OR MALE-FERN AND FILICIC ACID

These drugs are usually given in capsules. They are very commonly prescribed to be given in divided doses of 5 grains each, at intervals of 15 minutes. The last dose is followed, in three hours, by a saline cathartic. Castor oil must not be used as the fixed oils favor the absorption of the drugs. As aspidium owes its action to filicic acid, both drugs have the same poisonous effects, which are due to irritation of the alimentary canal and, if the drug is absorbed, stimulation and then depression of the central nervous system. Thus the common symptoms are: Nausea, vomiting, purging, twitching of the muscles and, sometimes, convulsions, followed by stupor, collapse and coma. If the patient recovers, nephritis is likely to follow from irritation of the kidneys during the elimination of the drug.

CHENOPODIUM

The action and poisonous effects of chenopodium are the same as those of other irritant volatile oils. When

used to cause the expulsion or destruction of hookworms, chenopodium is very commonly given through a duodenal tube. This tube is passed in somewhat the same manner as a stomach tube, but into the duodenum.[1] This method is used because it has been found that the ankylostoma infest the jejunum more than other parts of the intestines, and as chenopodium, like other volatile oils, is readily absorbed from the stomach and duodenum, enough does not always reach the jejunum to be effectual when the drug is taken by mouth. The oil is injected into the tube from a glass syringe and, after about 6 minutes have elapsed, which gives the oil time to diffuse through the jejunum, 2 or 3 ounces (60–90 c.c.) of a saturated solution of magnesium sulphate is injected through the duodenal tube, which is then removed. When given by mouth, chenopodium is given in capsules or on sugar, in divided doses, two hours apart. The last dose is followed in about 2 hours by a dose of castor oil containing about 30 minims of chloroform or else a saline cathartic.

CUSSO

Cusso has a bitter taste and is astringent and, because of its astringency, it is very irritating in the large doses used as a vermicide. Thus, it is likely to cause vomiting and diarrhea and, if these conditions are extreme, consequent collapse. As cusso usually acts as a purgative it is not, as a rule, necessary to follow its use with a cathartic.

KAMALA

This is usually administered in syrup. Kamala is particularly irritating to the intestinal tract and is likely to cause diarrhea. When it does so, the subsequent cathartic is usually omitted. Its poisonous effects are similar to those induced by aspidium.

[1] The method of passing a duodenal tube is described in most of the modern text-books of nursing procedure. It is only done by a doctor or a nurse who has been specially instructed in the technique of the procedure.

POMEGRANATE (GRANATUM) AND PELLETIERINE

These drugs are very toxic. They produce their poisonous effects chiefly by irritating the alimentary canal and, after absorption, paralyzing the motor nerve-endings in the muscles. The symptoms of poisoning are: Vomiting, purging, stupor, dimness of vision, extreme muscular weakness, collapse. The treatment is that used for irritant drugs.

PUMPKIN-SEED (PEPO)

These are the seeds of the ordinary pumpkin.

When the untreated seeds are used they are crushed and beaten with honey or syrup until in the form of an emulsion. Such a mixture is a harmless and fairly effective vermifuge for tape-worms. Squash-seed can be substituted.

SANTONIN

This is a very commonly used, but highly poisonous, lumbricide and patients receiving it need to be carefully watched. A varying amount of santonin is always absorbed and excreted through the kidneys and it gives the urine a yellow tinge.

Most of the symptoms of poisoning are due to (1) gastro-intestinal irritation; (2) stimulation of reflex centers; (3) some unknown effect upon the sense organs or their nerve-centers, it is not known which. The symptoms are: Vomiting, diarrhea, twitching and jerking of the muscles and, sometimes, convulsions, in which case death is likely to occur from interference with the action of the respiratory muscles. There are also likely to be hallucinations and delirium; derangement of the senses of smell, taste, hearing and vision. Partial blindness and a peculiar disturbance of color vision, known as *yellow sight* or *xanthopsia*, that causes all objects to have a yellow tinge, are particularly common. The treatment for poisoning is the same as for other irritant drugs and, in

addition, a bromide and inhalations of ether may be given to check convulsions.

SPIGELIA (PINK-ROOT)

This is usually given on sugar and the cathartic senna is very commonly given at the same time. If the senna is effectual no other cathartic is used, but a thorough purge is essential for, if absorbed, spigelia is very poisonous. It causes poisoning chiefly by depressing the central nervous system, the symptoms are: Flushing of the skin; weak, rapid pulse; muscular weakness and incoördination; disturbance of vision; stupor, collapse.

TURPENTINE

This is described under Volatile Oils. It is rarely used as a vermicide, because if it is given in large enough doses to destroy worms it is very irritating to the alimentary canal. When it is used, it is usually given beaten into an emulsion with olive or other oil, in the proportion of 1 part of turpentine to 2 or 3 of oil. To act as a vermifuge, it is sometimes used as an enema, in relatively small doses, ½ oz. or less, to a quart of soapsuds.

THYMOL

Thymol is a stearopten obtained from the oil of thyme. Its action is described under Volatile Oils. When used as an anthelmintic, it is generally given in divided doses, either in capsules or beaten into an emulsion in a syrup, *never in oil*, for this hastens its absorption. The purgative is generally given two hours after the last dose. Thymol is exceedingly poisonous. The symptoms of poisoning and its treatment are described under Volatile Oils.

ASTRINGENTS

Astringent action, as stated on page 47, implies shrinking or contraction of tissues; a condition that can be brought about by (1) contracting the blood-vessels in the tissue, as adrenaline and cocaine do; (2) extracting water from the tissues, an action characteristic of alcohol, glycerine, acids, and mineral salts; (3) combining with the protein of the protoplasm and precipitating it. In addition to causing contraction of the affected tissues, such an action, when not too pronounced, tends to lessen local secretions, to diminish the permeability of the superficial blood-vessels and to lessen the sensitiveness of sensory nerve-endings in the part with which the astringent comes in contact. If this action is pronounced, the affected tissues will be irritated and pain, inflammation and, sometimes, corrosion will follow.

With the exception of potassium chlorate, all the drugs usually classed as astringents act in the manner last described. Those which owe their astringent effects to other actions have more important uses and are elsewhere described.

The drugs classed as astringents are divided under two headings; viz., the vegetable or organic astringents, and the mineral or inorganic.

ORGANIC OR VEGETABLE ASTRINGENTS

The principal organic astringents are tannic acid, or tannin, and myrrh.

TANNIN (ACIDUM TANNICUM)

Tannin or tannic acid is a substance with a slightly acid reaction. It occurs in a number of plants, but is found

in largest amounts in growths named *nutgalls* that form on a species of oak, known as the *Quercus infectoria* or *gall oak-tree.*

Preparations and dosage of tannin:

For external use:

Glycerite of tannic acid, tannic acid ointment, styptic collodion, all which contain 20 per cent. tannic acid.

For internal use:

Tannic acid, 3–10 grs. (0.2–0.6 gm.).

Tannalbin, 15–60 grs. (0.1–4.0 gm.)
Protan, 15–30 grs. (0.1–2.0 gm.)
Tannacol, 15–30 grs. (1.0–2.0 gm.)
} *Combinations of tannic acid and protein.*

Tannigen, 3–10 grs. (0.2–0.6 gm.) (diacetyltannin).

Tannoform, 3–10 grs. (0.2–0.6 gm.) (formaldehyd and tannic acid).

Tannopin or tannon, 3–10 grs. (0.2–0.6 gm.) (hexamethylenamine tannin).

Preparations and dosage of drugs prepared from plants containing tannin:

Blackberry, fluidextract of, 1–2ʒ (4.0–8.0 c.c.).

Gambir, tincture of, 1ʒ (4.0 c.c.).

Kino, tincture of, 1–2ʒ (4.0–8.0 c.c.).

Logwood (Hæmatoxylon) extract of, 10–30 grs. (0.6–2.0 gm.).

Nutgall, tincture of, 1–2ʒ (4.0–8.0 c.c.).

Witch hazel, fluidextract of, 2ʒ (8.0 c.c.). This is more frequently used as an external application.

There are a number of other drugs which contain tannin, but they are no longer listed in the Pharmacopœia and are rarely used. Tannin is also contained in tea and an infusion that is allowed to stand for some time or a decoction may contain a considerable amount.

Fate of Tannin in the Body.—Tannin unites with the protein of food that is in the stomach, but, as digestion progresses, the compounds thus formed are broken up and the tannin set free. In the intestines some of the tannin is changed to gallic acid and both this and the tannin gradually unite with alkaline substances, forming gallates and

tannates. These are slowly, but fairly completely, absorbed and, it is thought, oxidized in the tissues. They have no effect after absorption.

Actions and Their Effects.—Tannin combines with: Proteins, alkalies, alkaloids, some glucosides, and the salts of the heavy metals. Except for its employment as a chemical antidote in the treatment of poisoning by alkaloids, the **therapeutic uses of tannin depend upon** the effects of its astringent action, which, as previously stated, is due to its action on the protein substances of the superficial cells of the tissues with which it comes in contact.

Tannin, when applied to the **unbroken skin,** tends to harden and dry the latter and thus it is of use in preventing bed-sores.

Applied to **bleeding surfaces** it tends to check the bleeding by coagulating the protein in the blood at the point of application, thus forming clots which block the openings of the severed vessels. This is known as *styptic action.*

Its action on **mucous membranes** is more pronounced than on the skin, and it lessens the secretion of mucus and the sensitiveness of the sensory nerve-endings in the part.

In the mouth tannin gives rise to a harsh, bitter taste, but in spite of this the secretion of saliva, as well as mucus, is lessened, because of the precipitation of the protein of the secreting cells; also, the mouth being particularly sensitive, there will be sensations of dryness, roughness and constriction.

If there is food **in the stomach** when tannin is taken, the effect on the gastric membrane will be less than in the mouth and the digestion of the food will be retarded; but as digestion progresses and the tannin is set free, it will have the same effect upon the gastric and intestinal membranes as upon other mucous membranes. As it tends to check secretion it makes the feces drier and retards their passage through the **bowel** and this and the lessened sensitiveness of the nerve-endings, which limits their stimu-

lation by material in the intestines, will overcome diarrhea or promote constipation. If, however, tannin is taken in large amounts, especially when there is no food in the stomach, it will cause so much change in the protoplasm of the membranes that it will induce irritation and, consequently, vomiting and diarrhea.

The above effects and, possibly, a slight degree of collapse, as the result of the vomiting and diarrhea, are the only **results of overdoses of tannin,** but, if relatively large amounts are taken constantly, as in strong tea that has been boiled or allowed to infuse for a long time, harmful changes are likely to be caused in the gastro-intestinal membrane which may seriously interfere with digestion and promote chronic constipation.

The newer compounds and the drugs containing tannin are now more commonly used than the uncombined tannin because they interfere less with digestion.

The principal therapeutic uses of tannin are: It is applied locally, in the form of a solution, ointment or glycerite to harden the skin and thus lessen the danger of pressure-sores; to check local sweating and bleeding; and to contract swollen gums.

As an ingredient of mouth washes and lozenges, it is used to contract relaxed membranes of the throat.

As an ingredient of suppositories or ointments, it is used to contract hemorrhoids.

It is given by mouth as an antidote in poisoning by alkaloids.

It is administered both by mouth and in enemata to check diarrhea.

MYRRH

Tincture of myrrh, dose, ½–1 ʒ (2.0–4.0 c.c.).

Myrrh is a resinous substance obtained from a species of balsam tree. It contains a volatile oil and has both astringent and carminative **actions.** Thus, though it contracts tissue as tannin does, it stimulates nerve-endings in the part and increases secretion and, if taken by mouth,

peristalsis. It is used chiefly as an ingredient of cathartics, as an expectorant and, generally in the form of a glycerite, it is used locally to contract swollen gums.

MINERAL OR INORGANIC ASTRINGENTS

The mineral or inorganic astringents are potassium chlorate, alum and salts of the heavy metals. Only a few of the latter, however, are used specially for their astringent properties, viz.: Bismuth, copper, lead, silver, and zinc.

POTASSIUM CHLORATE

(Symbol $KClO_3$)

Dose, 5–15 grs. (0.3–1.0 gm.).

As a mouth wash or gargle it is used in 2–6 per cent. solutions.

Troches of potassium chlorate each contain 5 grs. (0.3 gm.).

Action and Uses.—Potassium chlorate owes its astringent properties to its salt action (extraction of water). It is now rarely used except as an astringent mouth wash and gargle, in the treatment of catarrhal and relaxed conditions of the throat; for, if swallowed, it is readily absorbed and, after absorption, it unites with the hemoglobin of the blood, forming what is known as *methemoglobin* which interferes with the oxygen carrying property of the red cells and, in large amount, it will cause hemolysis (destruction of red cells).

Poisoning by potassium chlorate has occurred as the result of swallowing solution used for gargling. A mild form of poisoning will cause nausea and diarrhea (as the result of the irritation of the mucous membrane by the salt action of the drug) and diuresis and the urine may contain a reddish deposit, because of the presence of material due to the destroyed blood cells.

More pronounced poisoning, in addition to the above symptoms, will cause cyanosis, dyspnea (due to lack of oxygen), a rapid feeble, irregular pulse, giddiness, pro-

nounced weakness, and the diuresis may be followed by anuria, due to injury to the kidney cells, as well as to loss of fluid from the body.

The treatment for poisoning is the same as for other irritant drugs and, in severe poisoning, phlebotomy is sometimes performed in order to remove some of the useless blood, and this is replaced either by transfusing fresh blood or an intravenous injection of normal salt solution.

ALUMINIUM

(Symbol Al)

Aluminium is a tin-white, light, metal element. It unites readily with acids to form salts.

Preparations and dosage:

Alum (aluminium and potassium sulphate), 5–20 grs. (0.3–1.3 gm.).

Aluminium hydroxid, 5–20 grs. (0.3–1.3 gm.).

Aluminium acetate, Aluminium sulphate, Aluminol (Alumini naphthosolsulphonas) and dried or burnt alum are all used externally in percentages mentioned under Therapeutic Uses.

Fate in the Body.—Aluminium salts are only very slowly absorbed. After absorption they are excreted in the urine and bile.

Action and Effects.—Aluminium salts, like those of other metals, precipitate proteins with which they come in contact. As the result of this aluminium solutions are astringent and, they, thereby, act as antiseptics and, when applied to mucous membranes, raw surfaces and, to a slight extent, the skin, they contract the involved tissue and lessen its secretion. In the alimentary tract, these effects, in moderation, tend to overcome diarrhea but, if excessive, they will cause nausea, vomiting, and diarrhea. Dried alum is more astringent than the other preparations, because, in addition to its action on protein, it has a great avidity for water and extracts it from tissues with which it comes in contact. Aluminium salts are so

imperfectly absorbed that, even if used in poisonous concentration, they do not affect the tissues after absorption and, therefore, the only symptoms of poisoning will be those induced by severe local irritation of the part involved.

Therapeutic Uses.—Dried alum is used, dissolved in alcohol, 1:5 parts, to dry and harden the skin and thus prevent bed-sores. The other preparations are used, in ½–5 per cent. solutions, for their astringent and antiseptic properties, as douches, moist dressings for ulcers and similar conditions, and, as gargles, in the treatment of relaxed throat and to overcome salivation; 5–10 per cent. solutions of alum are sometimes used for bathing patients who perspire profusely. Alum crystals are touched to canker sores, such as occur in the mouth, to cause their shrinkage.

BISMUTH

(Symbol Bi)

Bismuth is a heavy, crystalline, brittle, metal element that, like other metals, combines with acids to form salts.

Preparations and Dosage:

Bismuth and ammonium citrate, 2–5 grs. (0.13–0.3 gm.).

Bismuth subcarbonate, 5–30 grs. (0.3–2.0 gm.) or for *x*-ray examinations 2–4 oz. (30.0–120.0 gm.).

Bismuth oxide, for *x*-ray examinations, 2–4 oz. (30.0–120.0 gm.).

Bismuth oxychloride, for *x*-ray examinations, 2–4 oz. (30.0–120.0 gm.).

Bismuth subgallate (dermatol), 5–20 grs. (0.3–1.3 gm.).

Bismuth subnitrate, 5–30 grs. (0.3–2.0 gm.).

Milk of bismuth (magma bismuthi), 1 (4.0 c.c.). This contains bismuth hydroxide and bismuth subcarbonate.

There are a number of **new preparations** of these; the most important ones are:

Airol (bismuth oxyiodide gallate).

Bismuth benzoate.

Bismuth cresolate.
Bismuth phenolate.
Bismuth salicylate.
Bismuth sulphocarbolate.
Dermol (bismuth chrysophenate).
Eudoxin (tetraiodophenolphthaleinate).
Orphol (bismuth naphtholate).
Thioform (bismuth dithiosalicylate).
Xeroform (bismuth tribromphenolas).

The common dosage of these preparations is 15–45 grs. (1.0–3.0 gm.).

Fate in Body.—The bismuth salts used in therapeutics are insoluble and therefore only very slightly absorbed through mucous membranes; they are absorbed more readily, however, from wounds and abraded surfaces such as ulcers and burns. The bismuth absorbed is excreted through the salivary glands, stomach, intestines and kidneys.

Actions and Effects.—As the salts of bismuth used in therapeutics are not soluble they do not combine with proteins to anything like the extent that the soluble salts of metals do and, therefore, they are only very slightly astringent and, if pure, they are not irritant.

When taken by mouth they form a coating on the walls of the stomach and intestines that is only gradually expelled, and while present protects them from irritating substances within the organs. This lessens nausea and diarrhea and, sometimes, it will check the excessive secretion of hydrochloric acid.

When applied to sores and wounds the bismuth salts, by forming a protective coat, lessen irritation from dressings and secretions and, by absorbing the wound secretions, they make conditions less favorable for bacteria and thus they act as antiseptics, but, because of their insolubility, as far as the bismuth is concerned, they do not destroy bacteria Many of the new preparations, however, contain phenols or other substance with germicidal properties and these have more decided antiseptic properties and

have greater power to retard the activity of bacteria in wounds and in the intestines.

Common therapeutic uses are: As protectives and absorbents on ulcers and similar sores. As protectives in gastric catarrh and ulcer. To lessen nausea and diarrhea. To allow of observing the activity of the gastro-intestinal tract—for this purpose the compounds indicated in the list of preparations are used, as they are even less likely than others to be absorbed or to act as irritants in large amounts. They are generally given in buttermilk or thick soup. Their value for this purpose depends upon their impermeableness to the *x*-rays, which makes them show as a dark shadow in *x*-ray photographs and thus, if photographs are taken at intervals, the rate at which material is forced through the gastro-intestinal tract can be ascertained.

Toxicology.—Poisoning is not common but it does occur, especially when large amounts of bismuth preparations are used on wounds.

The symptoms of poisoning are chiefly the result of conditions produced during the excretion of the bismuth. They are: Salivation, swelling and discoloration of the gums, tongue and throat; nausea; vomiting and diarrhea; sometimes, albuminuria and collapse.

The treatment consists in washing the part coated with bismuth with warm oil and, if necessary, taking means to prevent collapse.

COPPER (CUPRUM)

(Symbol Cu)

Copper is a heavy metal element.

Copper sulphate is the only official salt, dose (as an emetic) 4–10 grs. (0.25–0.6 gm.) in enough water to make a 1 per cent. solution.

Action and Effects.—Copper sulphate precipitates the protein of protoplasm and, thereby, it destroys bacteria and is astringent to mucous membranes and other soft tissues. Solutions above 1 per cent. will cause irritation

and concentrated preparations induce corrosion, *i.e.*, they are caustic.

A 1 per cent. solution taken by mouth will give rise to a harsh taste and produce a copious flow of saliva and, when swallowed, it will irritate the stomach and cause vomiting, but it will not induce as much nausea and depression as the majority of emetics.

Therapeutic Uses.—The crystals are used to touch exuberant granulations in wounds and, in the disease known as trachoma, on the eyelids. A solution of about 1 per cent. is used for irrigation in the treatment of conjunctivitis, vaginitis, urethritis, especially when the conditions are due to gonorrheal infection, and it is given internally as an emetic, especially in phosphorus poisoning.

The symptoms of poisoning are due to the irritation of the alimentary canal for the drug produces vomiting so promptly that very little is absorbed. They are: nausea, vomiting, purging, severe abdominal pain and, as the result of these conditions, more or less pronounced collapse. If a concentrated solution has been used, the vomitus and stools may contain blood and shreds of mucous membrane.

The treatment is that described on pages 68 and 69.

LEAD (PLUMBUM)

(Symbol Pb)

Lead is a heavy metal element which has a silvery luster, but tarnishes readily to a blue-gray color.

Preparations and dosage:

Lead acetate (sugar of lead), 1–5 grs. (0.06–0.3 gm.).

For external use there are a number of preparations the principal ones of which are: Solution of lead acetate; solution of lead subacetate (Goulard's extract), lead plaster and diachylon ointment. The plaster consists of lead oxide, soap and water; the ointment of lead plaster, olive oil and oil of lavender.

Administration.—When lead acetate is used for its effects in the intestine, it should be given in pill form, or,

preferable, in keratin capsules,[1] otherwise, it will act upon the stomach and, also, it will be partly absorbed and thus have less effect in the intestine where its action is needed.

Fate in the Body.—Lead is absorbed from abraded surfaces and mucous membranes. It passes from the blood into the tissues and is only slowly eliminated. It is excreted chiefly through the kidneys but also in the saliva and bile and through the intestinal wall.

Action and Effects.—Lead salts coagulate protein and are therefore astringent in dilute preparations and irritant in concentrated, but they are not as corrosive as some of the other metal salts. Because of their astringency they will check diarrhea and, when applied to an open sore as an ulcer or a burn, they form a coating over the surface that protects it from irritation and thus lessens pain and promotes healing.

Lead poisoning is one of the most common forms of occupational poisoning, lead being a constituent of paint, printers' type and of a number of substances used in a variety of industries. Also poisoning has occurred from drinking water that has stood for a long time in lead pipes and by eating food that has been preserved in cans for which lead solder has been used.

The symptoms, known as plumbism, vary somewhat, but common ones are: Loss of appetite, anemia, frequent headaches, constipation, attacks of intestinal colic that will be associated with nausea, vomiting and faintness; congestion of the membrane of the mouth which, unless the mouth and teeth are kept very clean, may result in inflammation of the gums and caries of the teeth, also a blue line (due to the depositing of lead salts) may form at the junction of the gums and teeth; tremor, especially of the tongue and fingers; and, later paralysis, especially of the extensor muscles controlling the wrists, which results in the typical condition of the wrists known as *wrist-drop;* neuritis and the inflammation of the optic

[1] The keratin is dissolved by the alkaline juices of the intestine but not by the gastric juice as ordinary capsules are.

nerve may result in blindness. Also, as the result of injury to the tissues of the organ of the body, conditions such as arteriosclerosis and nephritis, may be induced. Lead poisoning occurring in a pregnant woman is likely to result in abortion from death of the fetus.

The treatment consists in removing the cause and hastening excretion by the use of diuretics, diaphoretics and cathartics. Magnesium sulphate and sodium sulphate are the cathartics chiefly used because their sulphate ion combines to form lead sulphide which is inert and lemonade containing about 10–15 drops of dilute sulphuric acid is given two or three times a day. The free use of these antidotes by people whose employment exposes them to lead poisoning is advised to prevent poisoning. Other precautionary measures are: To cover abraded surfaces through which the lead could be absorbed; to wash the hands thoroughly before eating; to be especially careful of the mouth and teeth.

SILVER (ARGENTUM)
(Symbol Ag)

Silver is a heavy, rather soft, whitish metal. Like other metals it will combine with acids to form salts. The official salt of the U.S.P. is that formed with nitric acid—*i.e.*, silver nitrate, known also as lunar caustic, a name given to it in ancient times by the Arabs, who used this salt in the treatment of nervous disorders because they believed that both the nervous system and silver were influenced by certain similar phases of the moon (luna).

Preparations and Dosage.—Silver nitrate can be purchased moulded into sticks, which facilitates its use in solid form. What are known as sticks of *mitigated silver nitrate* contain potassium nitrate as well as lunar caustic. Silver nitrate is used in 2 per cent. solutions for local application to the eyes; in 1–5 per cent. solutions for local application to the throat, gums, nipples, and in 0.1–1.0 per cent. solutions for the irrigation of mucous-lined cavities such as the rectum, urethra, bladder, vagina.

There are also a large number of new organic preparations of which the principal ones are:

Actol (*lactate of silver*), used in 1:500 solutions.

Albargin (*gelatose and silver*), used in 1–5 per cent. solutions.

Argentamine (*silver phosphate and ethylenediamine*), used in 1–4 per cent. solutions.

Argonin (*casein and silver*), used in 2–20 per cent. solutions.

Argyrol (silver oxide and vitellin), used in 10–25 per cent. solutions.

Collargol (silver and albumin), 1 gr. (0.06 gm.) diluted to ½ per cent., is given intravenously, and, in ointments 10–15 per cent., it is given by inunction.

Ichthargan (silver and sulphur), used in ¼–3 per cent. solutions.

Itrol (citrate of silver), used as a disinfectant powder and in 1:300–1:500 solutions.

Novargan (silver and proteins), used in 10–15 per cent. solutions.

Protargol (albumin and silver), used in 1:1000–1:2000 solutions for irrigations and in 1–10 per cent. solutions for local applications.

Action and Its Effects.—By coagulating the tissue protein, silver nitrate in dilute preparations, acts as an astringent, but it is also irritant, and, in concentrated form, caustic. Its action is superficial, however, as it has little penetrating power and it is not readily absorbed. Its action is more marked on mucous membranes and in wounds than on the skin, but even the latter gives evidence of irritation—redness and itching—when exposed to the influence of moderately concentrated preparations and is blistered by concentrated ones.

By precipitating the protein of bacterial protoplasm, silver nitrate acts as a disinfectant, a 2 per cent. solution will destroy streptococci and a 0.1 per cent. solution will destroy gonococci in about 5 minutes.

Silver salts are reduced (*i.e.*, they lose some of their

oxygen) when exposed to light and thereupon become a dark gray color, thus they stain tissues, linen, etc. with which they come in contact. A stain can be removed by covering it with tincture of iodine and washing off the latter with a solution of sodium hyposulphate or ammonia water.

Silver salts are only very slowly absorbed and are deposited in the tissues in an inert form. When present in sufficient quantity under the skin and mucous membranes they impart a dark-grayish hue to the body, a condition known as *argyria*. It is incurable because the silver is not eliminated. They have no other effect after absorption.

The organic preparations, especially those combined with protein, are less irritating to the tissues than silver nitrate but they are not as efficient germicides.

The chief therapeutic uses of silver preparations are: As antiseptic irrigations for mucous-lined cavities, especially in the treatment of infection due to the gonococci.

As local application for the eyes in the treatment of ophthalmia and, especially to the eyes of the new-born, as a prophylactic measure to prevent ophthalmia. Silver nitrate and argyrol are the preparations most commonly used.

Silver nitrate is used to cauterize exuberant granulations in wounds, and to destroy warts and similar growths.

Collargol is sometimes injected intravenously in the treatment of septicemia.

The symptoms of poisoning by silver are due to the conditions produced by the local irritation and are the same as those described on page 64.

Sodium chloride is the chemical antidote for silver poisoning because it interacts with other silver salts forming an insoluble, non-irritant compound—silver chloride. The rest of the treatment is that usual for poisoning by irritants.

Because of the tendency of silver salts to interact with sodium chloride, distilled water should be used for **diluting silver preparations.**

ZINC (ZINCUM)

(Symbol Zn)

Zinc is a rather heavy bluish-white metal element.

Preparations and dosage:

Zinc sulphate, 10–30 grs. (0.6–2.0 gm.). It is dissolved in sufficient water to make a 1 per cent. solution when used as an emetic.

Zinc bromide, zinc iodide, and zinc valerianate are used in doses of 1–2 grs. (0.06–0.12 gm.). *These owe their properties to their acid iron and are not astringent.*

For external use: Zinc acetate, zinc carbonate, zinc chloride, zinc oxide and zinc stearate.

The action and uses of zinc sulphate are similar to those of copper sulphate. **The chloride** is more irritant than the other preparations and is used chiefly as a caustic and, in 1 per cent. solutions, as a disinfectant. **The acetate, carbonate, oxide and stearate** are only mildly astringent and antiseptic, they are used chiefly as ingredients of dusting powders for the skin and in ointments for use on burns, ulcers and the like. In this form they serve to protect wounded surfaces from irritation by dressings and they lessen wound secretions, thus making conditions less favorable for the activity of bacteria.

At one time zinc salts were extensively used internally in the treatment of **nervous diseases** under the supposition that they were nerve sedatives, but this has been shown to be erroneous except when, as in the case of the bromide and valerianate, the acid ion of the salt has such an effect.

SALTS OF THE HEAVY METALS THAT ARE MORE COMMONLY USED FOR OTHER EFFECTS THAN THOSE DUE TO THEIR ASTRINGENT QUALITIES

IRON (FERRUM OR FERRI)

(Symbol Fe)

Iron is a metal element found in many ores and minute amounts of organic combinations are contained in many plant and vegetable cells. In the animal body it occurs chiefly in the hemoglobin of the red blood-corpuscles, for the formation and functioning of which it is essential. The function of the red blood-corpuscles, it will be remembered, is to absorb oxygen while the blood is passing through the lungs and part with it to the tissues.

Preparations and dosage:

For external use:

Iron chloride, used in 10–20 per cent. solutions.

Iron subsulphate (*Monsel's solution*) contains 16 per cent. iron.

For internal use:

Aloes and iron, 3–10 grs. (0.2–0.6 gm.).

Blaud's pills, 1–5 pills, (*each pill contains 1 gr. iron sulphate with sodium carbonate, tragacanth—sugar and glycerin*).

Compound iron mixture (*Griffith's mixture*), ½–1 oz. (15.0–40.0 c.c.).

Iron and ammonium acetate solution (*Basham's mixture*) (15.0–30.0 c.c.).

Iron (ferric) carbonate (Vallet's mass), 4 grs. (0.25 gm.).

Iron chloride, tincture of (*muriated tincture of iron*), 5–30 m. (0.3–2.0 c.c.).

Iron citrate, 1–5 grs. (0.06–0.3 gm.).

Iron iodide, pills of, 1–3 pills (*each pill contains ½ gr. reduced iron with iodine, acacia, balsam of tolu and licorice*).

Iron iodide, syrup of, 5–30 m. (0.3–2.0 c.c.).

Iron and potassium tartrate, 5–15 grs. (0.3–1.6 gm.).

Iron phosphate (soluble) (1–5 grs., 0.06–0.3).

Reduced iron, 1–5 grs. (0.06–0.3 gm.).

Iron and quinine citrate, 5–10 grs. (0.3–0.6 gm.).

Iron quinine and strychnine phosphate, 1–2 ʒ (4.0–8.0 c.c.).

Iron and strychnine citrate, 2–5 grs. (0.13–0.3 gm.).

New non-official preparations:

Dialyzed iron, 20–40 m. (1.3–2.6 c.c.).

Ferratin, 8 grs. (0.5 gm.) (*egg albumin and iron*).

Ferro-mangan solution, 1–4 ʒ (4.0–16.0 c.c.) (*iron, peptones and manganese*).

Ferrous lactate, 3–15 grs. (0.2–1.0 gm.) (*a salt of iron and lactic acid*).

Hæmaboloids, ½ oz. (15.0 c.c.) (*iron blood-proteins and bone marrow*).

Ovoferrin, 2–3 (8.0–12.0) (*serum albumin and iron*).

There are a number of similar preparations but the above are the ones that are most commonly used.

Preparations of iron used as arsenic antidotes:

Ferric (iron) hydroxide. *This is prepared by adding ammonia water or a solution of sodium carbonate to tincture of iron chloride or iron sulphate, until a precipitate ceases to form. The resulting mixture is strained through filter paper and the precipitate is washed by pouring water over it (to remove the alkali). The washed precipitate is usually given in milk. It can be given in large quantities, but its use must be followed by lavage. It requires 8 grains of the hydroxide to neutralize 1 gr. of arsenic.*

Ferric hydroxide with magnesium oxide. *This is prepared by combining iron sulphate, magnesium oxide and water. It can be used freely.*

Administration.—Iron preparations are given after meals. They should be well diluted and milk and syrups are good diluents. Liquid preparations should be given through a tube, for iron discolors the teeth, and, after iron is used as a mouth wash, the teeth must be well brushed

immediately. Silver spoons should never be used for measuring or mixing iron preparations, for they are discolored by the iron.

Fate in the Body.—The fate of inorganic iron in the body has been a matter of much difference of opinion for many years. For a long time, as the result of experiments it was thought that inorganic iron could not be synthesized into the necessary organic combinations in the animal body and that medicinal preparations merely acted in some unknown way as a stimulant to the use of food iron. However, more recent experiments have given rise to the following theory: The iron preparations used in medicine undergo some change either in the stomach or duodenum. The resulting compounds are absorbed, though probably imperfectly, and pass through the portal vein to the spleen. Whether they undergo any change in this organ or not is not known, but, if so, it is not an essential one for there is no alteration in the use of iron after excision of the spleen. Later, the iron is gradually taken up from the spleen by the blood and deposited in the liver and bone marrow. If the amount of iron in the body is not sufficient for the formation of the normal amount of hemoglobin, that taken as medicine will be synthesized into ferratin and, eventually, hemoglobin, in the liver. If, however, the iron supply of the body is adequate, the liver slowly yields up this store of iron to the blood and it is carried to the intestines and kidneys, especially the former for excretion.

Actions.—Iron coagulates protein and thus is astringent and somewhat irritating, though not as much so as some of the other metals.

When taken by mouth, iron gives rise to a metallic taste and acts as an astringent and, in large or concentrated doses, as an irritant in the alimentary canal.

Its actions after absorption are indicated in the paragraphs describing its occurrence and fate in the body.

Effects of Actions.—**On the unbroken skin,** iron has no effect. **Applied to bleeding areas,** it, by coagulating the

protein in the blood at the point of application, favors the formation of a clot and thus tends to stop bleeding, *i.e.*, it acts as a styptic.

When taken by mouth, because of the stimulation of taste-buds, iron may induce a slight transitory increase in the flow of saliva, but its astringent action checks secretion and causes the contraction of the mucous membrane of the alimentary tract. In the intestine these effects tend to promote constipation. To avoid this, cathartic drugs are sometimes included in iron preparations.

Excessive or concentrated doses of iron may cause nausea and vomiting.

The effects of the drug after absorption will be evident only if anemia exists as, otherwise, the iron will, as previously stated, be excreted unused. In anemia the iron tends to overcome the condition, by promoting the formation and functioning of hemoglobin, and, consequently, improving nutrition and the general body health. For the body can not be in a healthy condition unless it is supplied with enough oxygen for the normal oxidative processes to be carried on properly and, under ordinary circumstances, the amount of oxygen absorbed depends upon the quantity of hemoglobin in the blood. By improving the condition of the blood and the general body health iron helps to overcome amenorrhea. Thus it acts as an emmenagogue.

Iron is used in therapeutics as a hematinic and, because of its hematinic properties, as an emmenagogue.

As the iron of food is the kind that the body needs and it does not induce the undesirable effects of inorganic iron, it is most important that, when iron is needed, the amounts of foods containing relatively large quantities of iron be used as freely as possible. These include the yolk of eggs and green vegetables.

The symptoms caused by the excessive use of iron preparations are due to the action of the iron on the alimentary canal, they are: Nausea, vomiting, and constipation and, due to these effects, malaise. The combina-

tions of iron and protein are said to be less astringent and, therefore, less constipating than others.

MANGANESE (MANGANUM)

Manganese is a hard grayish metal that resembles iron. It is contained in animal and some vegetable tissues in minute quantities, but it does not seem to be an essential constituent of protoplasm.

Preparations and dosage:

Manganese dioxide, 1–10 grs. (0.06–0.6 gm.).

Calcium permanganate, used in dilutions of 15 grs. (1 gm.) to a pint for antiseptic irrigations.

Potassium permanganate, ½–3 grs. (0.03–0.2 gm.) and, for irrigations, in dilutions of 1:500–1:1000.

Preparations of iron and manganese are classified with the iron preparations.

Actions and Uses.—Manganese is sometimes given with iron because it seems to hasten the absorption and the utilization of the former, but how the manganese does this is not known.

The permanganates part with their oxygen readily and thus serve as oxidizing agents, *i.e.*, their oxygen unites with many substances and thereby decomposes them. By this means the permanganates will, to some extent, destroy bacteria and act as deodorants and as chemical antidotes in opium and morphine poisoning and in poisoning by glucosides.

MERCURY (HYDRARGYRUM)

(Symbol Hg)

Mercury, known also as *quicksilver* is, in its pure state, a silver-colored, heavy, liquid metal that is easily volatilized. It occurs in nature chiefly as the sulphide (HgS) known as *cinnabar.* Like other metals it will combine with acids and form salts; some of its preparations notably mercuric chloride (commonly known as corrosive sublimate and bichloride of mercury), are made by a process of

sublimation. For example, **mercuric chloride** ($HgCl_2$) **is made** by heating a mixture of mercuric sulphate and common salt (sodium chloride) whereupon a chemical reaction takes place in which the mercury combines with the chlorine (forming mercuric chloride) and the sodium with the sulphur. The mercuric chloride, being volatile while hot, passes as it forms into the receptacle provided for it where, on cooling, it is deposited as a white powder. **Mercurous chloride** (HgCl) or calomel, **contains** less chlorine than the bichloride, but it is easily decomposed by light and a portion will then be changed to the more stable, but also more poisonous, mercuric chloride. Therefore, when calomel is kept in bottles the latter must be of colored glass.

Mercury compounds are incompatible with alkalies, soaps, proteins and many salts. For this reason solutions are best made with distilled water, and before a mercurial preparation is used on the skin, the part must be thoroughly cleansed, and all trace of soap must be washed off. For the same reason a solution is not to be used if it becomes contaminated with soap, as it can not then be relied upon to serve its purpose.

Preparations and dosage:

Bichloride of mercury (corrosive sublimate), $\frac{1}{60}$–$\frac{1}{10}$ gr. (0.0011 gm.). As an antiseptic irrigation for accessible body cavities a 1:10,000 solution is used; for a skin disinfectant a 1:1000 solution.

Blue mass, 2–10 grs. (0.13–0.6 gm.). *Contains 33 per cent. mercury combined with glycerine, honey, licorice and flavoring substances.*

Calomel (mild mercurous chloride), common dosage 1–3 grs. (0.06–0.2 gm.) but larger doses are sometimes used. See under Cathartics.

Mercury with chalk (gray powder), 2–10 grs. (0.13–0.6 gm.). *This is similar to blue mass, but contains chalk which makes it less irritant.*

Mercuric iodides and arsenic, Donovan's solution, 5–15 m. (0.3–1.0 c.c.).

Red iodide, or biniodide, of mercury, 1/30–1/15 gr. (0.002–0.004 gm.).

Yellow iodide, or protiodide, of mercury, 1/10–1 gr. (0.6–1.0 gm.).

Ointments:

Ointment of ammoniated mercury. Mercurial or blue ointment.

Mercuric nitrate ointment.

Red mercuric oxide ointment. Ointment of yellow mercuric oxide.

Non-official preparations:

Mercuric benzoate, 1/4–1/2 gr. (0.015–0.03 gm.).

Mercuric salicylate, 1/20–1/10 gr. (0.003–0.006).

Mercuric succinimide, 1/20–1/10 gr. (0.003–0.006).

Mercurol (hydrargyri nucleinas), 1/2–2 grs. (0.03–0.13 gm.).

For External Use.—Bichloride of mercury, used in solutions of 1:10,000 for irrigation of accessible body cavities, and in 1:1000 solutions for disinfection of the skin.

Black wash, this consists of calomel dissolved in lime-water in the proportion of 1 dram to 1 pint.

Harrington's solution, used as a skin disinfectant, consists of approximately 7 parts bichloride of mercury; 1 part hydrochloric acid; distilled water 37 parts; and alcohol 80 parts.

Mercuric cyanide, used in 1:4000 to 1:2000 solutions.

Mercuric oxycyanide, used in 1:5000 to 1:3000 solutions.

Potassium mercuric iodide, used in 1:5000 to 1:1000 solutions.

Sublamine (mercuric sulphate ethylenediamine) used in 1:1000 solutions.

Yellow wash, *a solution of bichloride of mercury in lime-water, in the proportion of 1/2 dram to 1 pint* (2.0 *gm. to* 500 *c.c.*).

For intravenous and intraspinal injections:

Mercurialized seras. These consist of either human or horse serum containing the required dose of bichloride, or other preparation, of mercury.

Administration.—For internal effects, mercurial preparations are given by: Mouth; inunction; inhalation; subcutaneous, intramuscular, and intravenous injections; and, in the treatment of tabes, intraspinal injection.

Fate in the Body.—When volatilized, mercury is readily absorbed through the lungs and mucous membranes and to some extent through the skin. When it is broken into minute globules, as it is in ointments, mercury is fairly readily absorbed even through the skin, especially if it is rubbed in (inunction). The soluble preparations are quickly absorbed from subcutaneous tissues, wounds, the mucous membrane of the stomach and intestines and, though probably less readily, other mucous membranes. The relatively insoluble preparations (calomel, blue mass and gray powder) are, unless volatilized, not as easily absorbed as the more soluble ones and thus, when taken by mouth, a considerable portion of each dose is eliminated in the feces without being absorbed. After absorption, mercury becomes very generally distributed throughout the body and a considerable portion of each dose is retained for some time. Thus, though a small amount may be found in the urine three or four hours after a dose has been taken, it may be several days before the entire amount is eliminated. In fact, mercury has been found in the tissues of patients who have died of mercurial poisoning when death has not occurred until three weeks after the poison was taken. Mercury is eliminated chiefly through the kidneys and the wall of the large intestine but also in the saliva and sweat and, slightly, in the gastric juice and bile. When a woman is pregnant, mercury may pass through the placental circulation to the fetus.

Actions.

The most marked property of mercury is its power to combine with proteins forming a precipitate known as *albuminate of mercury*. Because of this action, even dilute preparations are astringent and irritant and concentrated ones are corrosive.

Single therapeutic doses will have little **effect after absorption** except upon the organs through which they are eliminated, which they are likely to irritate, but when, as the result of small doses, mercury accumulates in the tissues to a moderate degree, it appears to have a slight stimulant effect upon cells, especially the red blood corpuscles. Poisonous doses are particularly destructive to the organs through which elimination occurs, nerve tissue and the red corpuscles.

There is some difference in the action of the various preparations, but this is chiefly dependent upon their degree of solubility and thus it varies in degree, rather than in nature, the soluble preparations being much more irritant than the relatively insoluble ones.

Mercury affects the protoplasm of bacteria in the same manner as human tissue and it, apparently, is especially toxic for the *spirochæta pallidum*, the organism that causes syphilis.

Effects of Actions:

On Bacteria.—Mercury is a germicide. A solution of bichloride of mercury has been found to kill bacteria, not spores, after an exposure of ½ hour and a solution of 1:500 to kill most types of spores after an exposure of 1 hour, provided the bacteria and spores are not protected in any way from the influence of the mercury. A solution of 1:10,000 acts as an antiseptic. However, the spirochæta pallidum is the only organism producing disease in man that, up to the present time, it has been found mercury can be counted upon to destroy in the interior of the body, when used in amounts that will not injure human tissues. To destroy the spirochæta it is necessary for the mercury or a substitute, as arsenic, to be constantly present in the body until the symptoms of syphilis are overcome.

Though bichloride of mercury is an excellent germicide its use as a disinfectant is limited because: It corrodes metal, it stains linen, it is too irritant to tissues in disinfectant strengths to be of much service for the irrigation of wounds or infected body cavities and it unites with the

protein in the discharges of wounds and in excreta forming an albuminate of mercury that is useless as a disinfectant and coats the bacteria, thereby protecting them from the influence of any uncombined solution. The new preparations, potassium mercuric iodide, mercuric cyanide and mercury oxycyanide are not as injurious to the tissues as bichloride and they do not corrode metal, but, with the exception of the potassium mercuric iodide, they are not as efficient disinfectants. The potassium mercuric iodide, however, is a more powerful germicide and, as it does not form inert compounds with organic matter, it is considered more suitable than bichloride for use about the body and it will disinfect excreta.

The mercurial disinfectants, especially the bichloride, tend to cause roughness and discoloration of the skin and when bichloride is in contact with the skin for any length of time it is likely to cause an eruption that may appear, not only at the part of application but over a considerable area. Such an eruption may persist for weeks and reappear repeatedly after it has been apparently cured. A skin eruption may also follow the internal use of mercury due, probably, to the irritation induced by the mercury during its excretion.

Mucous membranes and raw tissues are readily corroded by concentrated mercurial preparations and they become shrunken, contracted and irritated when subjected to the influence of dilute ones. Therefore, subcutaneous and intramuscular injections cause pain and, in spite of the astringent effect, local congestion.

In the mouth mercury gives rise to a metallic taste and this, as well as the irritant action of the mercury on the salivary glands during excretion, increases the flow of saliva.

In the alimentary tract, mercury inhibits the activity of bacteria, increases peristalsis and, sometimes, especially in large doses, causes nausea and vomiting. Also, it increases the excretion, but not the secretion of bile. This is thought to be due to the increased vigor of the duodenal

peristalsis which influences the communicating bile ducts, causing them to discharge their contents. The soluble mercurial preparations, which are readily absorbed, have, in therapeutic doses, less effect on the intestine than the more insoluble ones—calomel, blue mass and gray powder which, though they are less irritating, remain in the bowel for some time. Thus, the soluble preparations are more commonly used for their effects after absorption and the relatively insoluble ones are those chiefly used as cathartics.

After the absorption of a single therapeutic dose, the only effect usually observed is a slight diuresis, due to the irritation of the kidney cells by the mercury during its excretion; occasionally, the saliva is also increased.

After therapeutic doses have been used for a short time, there is likely to be an increase in the number of red blood-corpuscles and, consequently, lessening of anemia, and a general improvement of the person's health, but it is not known if these effects are due to the stimulation of the body cells, which improves their nutrition, or solely to the destruction of the organisms causing ill health, for mercury is seldom used continuously except in the treatment of syphilis. As previously stated, it will, by destroying the spirochæta, cure the conditions existing in the first and second stages of syphilis. Undesirable effects that are likely to occur when mercury has been used for some time are described under mercurialism.

Common therapeutic uses of mercurial preparations are: As skin disinfectants for surgical purposes and in the treatment of parasitic diseases.

As specifics in the treatment of the first and second stages of syphilis.

In disinfectant douches and irrigations, the potassium mercurial iodide is now most commonly used for this purpose.

As cathartics, calomel, blue mass and gray powder.

Toxicology.—Both acute and chronic poisoning by mercurial preparations are common. **Acute poisoning is generally due** to taking bichloride of mercury, either by

mistake or with suicidal intent. To avoid mistakes, the law now requires that bichloride tablets and solutions be colored. Acute poisoning has also been caused by the retention of solutions used for the irrigation of wounds or for vaginal douches. **Chronic poisoning or mercurialism** is generally the outcome of the continued use of a mercurial preparation in the treatment of syphilis or of the inhalation of mercurial fumes while working in industries in which mercury is used.

The symptoms of poisoning are due chiefly to the action of the drug on the organs through which it is excreted and, sometimes, its action on nerve tissue and the red blood-corpuscles and, if it is taken in concentrated form, its local action before absorption.

The symptoms of acute poisoning when a concentrated preparation is taken by mouth are: A harsh, metallic taste, pain in the alimentary tract, nausea, vomiting, diarrhea and tenesmus, with blood and, after a short time, shreds of membrane in the vomitus and stools. There may be convulsions and there will be a condition of collapse with weak, thready, irregular pulse; irregular, shallow, rapid breathing; cold, clammy skin. The individual may remain conscious or may pass rapidly into coma. Death may occur almost at once from shock, but the patient may live for two or three weeks and then die from exhaustion or uremia. If death does not occur at once conditions similar to those in chronic poisoning will follow and, as the result of renal irritation, the urine will contain albumin and casts, shreds of epithelium and, sometimes, sugar, also the excretion of urine will be much diminished and there may be suppression.

When a poisonous amount of mercury is taken in dilute form either by mouth or through other channels the corrosion of the alimentary tract is less marked, but, as much of the mercury is excreted through this channel, there will be an intense inflammation, and the symptoms induced will be those of severe chronic poisoning.

The symptoms of chronic poisoning (*mercurialism*) are:

A constant metallic taste in the mouth; salivation (excessive flow of saliva), stomatitis (inflammation of the mouth) which, if severe, may result in discoloration, ulceration and gangrene of the gums, tongue, interior of the cheeks and lips, with loosening of the teeth. In serious cases there will be nausea, colic, diarrhea, digestive disturbances (because of the congestion of the alimentary tract), the breath is fetid and foul and anemia develops. The secretion of urine is generally increased in the early stages but, later, it is diminished and the urine is then likely to contain albumin and casts. As the result of these conditions there will soon be a loss of weight, muscular weakness and cachexia. The temperature may be subnormal or there may be fever. If the nervous tissue becomes affected the individual is likely to be-become extremely irritable; to suffer from hallucinations, neuritis and tremors and paralysis of groups of muscles, especially the extensors of the hands and feet.

The first aid treatment for acute poisoning consists in lavaging the part through which the drug was taken (stomach, wound, etc.) and if taken by mouth, administering copious drinks of milk and white of egg (the albumin unites with mercury thereby forming an albuminate of mercury, which is not corrosive) and the usual means are taken to prevent shock. The subsequent treatment varies. The following description of a régime that is now very commonly employed for both acute poisoning and severe mercurialism was copied from the December (1916) number of Progressive Medicine.

"(1) The patient is given every other hour 8 ounces of the following mixture: Potassium bitartrate, 1 dram; sugar, 1 dram; lactose, ½ ounce; lemon juice, 1 ounce; boiled water, 16 ounces. 8 ounces of milk are administered every alternate hour. (2) The drop method of rectal irrigation with a solution of potassium acetate, 1 dram to the pint, is given continuously. (3) The stomach and intestine are lavaged twice daily. (4) The patient is given a hot pack daily."

The care of the mouth is of extreme importance and consists in keeping it clean and using astringent mouth washes, such as potassium chlorate and myrrh.

The usual treatment for mild mercurialism includes the above care of the mouth, the liberal use of water as a beverage, in order to flush the kidneys, and of milk and white of egg to soothe the irritated alimentary tract.

Care of the mouth is also **an important prophylactic measure** because the gums are easily irritated by the mercury excreted in the saliva and some individuals are salivated by a very small amount of mercury.

ARSENIC (ARSENUM)

(Symbol As)

Arsenic is a steel-gray, solid element. It resembles metals in appearance, but it is brittle and easily powdered. **It occurs** in considerable quantities in nature both uncombined and in the form of sulphides, oxides and other compounds. **When heated** it sublimes, *i.e.*, it becomes gaseous without melting and as the vapor cools it condenses to a solid. Arsenic unites with hydrogen and oxygen in different proportions and thereby gives rise to different acids. Of the inorganic acids, it is the arsenous or arsenious (AsH_3O_3) and the arsenic (AsH_3O_4) acids that are used in medicine. Also, an acid known as *cacodylic acid* is prepared from arsenic and certain organic compounds, salts of which (cacodylates) are now much used, as well as a number of other compounds of arsenic and organic substances.

Preparations and dosage:

Arsenous acid preparations:

Arsenous acid (*known also as arsenous acid and arsenic trioxide*), $\frac{1}{60}$–$\frac{1}{12}$ gr. (0.0011–0.005 gm.).

Arsenous acid solution, 2–8 m. (0.13–0.5 c.c.).

(*This is* 1 *per cent. arsenous acid in dilute hydrochloric acid.*)

Arsenous iodide, 1/20–1/5 gr. (0.003–0.3 gm.).

Donovan's solution (*Solution of mercuric and arsenous iodides*), 5–15 m. (0.3–1.0 c.c.).

Fowler's solution (*Solution of potassium arsenite*), 2–8 m. (0.13–0.5 c.c.).

Arsenic acid preparations:

Sodium arsenate, 1/60–1/20 gr. (0.0011–0.003 gm.).

Solution of sodium arsenate (*Pearson's solution*), 1–10 m. (0.06–0.6 c.c.).

Organic preparations:

Arsacetin (acetyl-atoxyl), 3/4 gr. (0.04 gm.).

Arsenophenylglycin, 12 grs. (0.8 gm.); *it is given by hypodermic.*

Arsenstriferrin, 5 grs. (0.3 gm.). *This is a compound of arsenic, iron, phosphorus and albumin.*

Atoxyl (*sodium arsanilate or sodium aminophenyl arsonate*), *contains 26 per cent. arsenic,* 1–5 grs. (0.06–0.3 gm.); *it is given by hypodermic.*

Cacodylate of calcium, 3/4 gr. (0.045 gm.).

Cacodylate of iron (*ferric cacodylate*), 1/4–1 1/2 grs. (0.015–0.1 gm.).

Cacodylate of sodium, 1–3 grs. (0.06–0.2 gm.).

Elarson, 1/8 gr. (0.008 gm.). *This is a lipoid-like combination of arsenic.*

Neosalvarsan or *neo-arsphenamine,* 5–15 grs. (0.3–1.0 gm.).

Salvarsan, *arsenobenzol, arsphenamine,* or 606, 5–10 grs. (0.3–0.6 gm.).

Soamin (*sodium arsanilate*), 1–5 grs. (0.06–0.3 gm.) *contains 22 per cent. arsenic; it is given by hypodermic.*

Administration.—Arsenic preparations given by mouth should be well diluted and given after meals. Fowler's solution is very commonly diluted with milk. When Fowler's solution is given by hypodermic it should be diluted with 2 parts of sterile water. Arsenophenylglycin, atoxyl and soamin are always given by hypodermic as they are decomposed by the gastric juice. Neosalvarsan and salvarsan are usually given intravenously.

Fate in the Body.—Arsenic preparations are readily absorbed from subcutaneous tissues, mucous membranes and raw surfaces and slightly through the unbroken skin. After its absorption arsenic soon passes from the blood into the tissues and is very generally distributed throughout the body, it has even been found in the spinal fluid when given in large amounts. It is retained in the tissues for some time and thus its elimination is very slow. For this reason it is likely to cause cumulative poisoning, though, as shown under toxicology some individuals establish a remarkable tolerance for the drug. It is excreted chiefly in the urine, but also through the wall of the large intestine, and the other excretory channels, and in the milk when the mammary glands are active. Also it has been found in the secretions of the scalp and in the hair.

Actions.—Most arsenic compounds, including those used in therapeutics are protoplasmic irritants that, in concentrated preparations, destroy tissues by inducing inflammation and fatty degeneration. Their action is more inimical to animals and to the higher types of microorganisms, such as the spirochæta and protozoa, than to bacteria. The arsenous acid preparations are more toxic than the arsenic acid compounds and the organic preparations, being only slowly decomposed, are less irritant than the latter; they are, in fact, the result of much experimental work to obtain compounds having the good, without the bad, effects of arsenous acid. Salvarsan is commonly known as 606 because the inventor (Ehrlich) made that many preparations before he obtained a compound that contained enough arsenic to destroy the spirochæta pallidum (the cause of syphilis) without necessarily injuring human tissues. Though it is customary to refer to the **arsenic action**, the element arsenic has not the irritant actions of its compounds and is not toxic.

Apart from their irritant property, which, in moderation, may act as a tissue stimulant, and their power to destroy certain microörganisms that invade the body,

practically nothing is known of the manner in which the arsenic preparations produce their effects.

Effects.—Arsenic is especially **toxic to the organisms** causing syphilis and malaria and certain tropical diseases caused by organisms of similar types, but it does not affect the malarial protozoan as readily as quinine.

Arsenic only affects the unbroken **skin** when it is kept in contact with it for a considerable time, in which case it may give rise to congestion and, possibly, the formation of vesicles and pustules and even ulceration.

The mucosa of the alimentary tract of individuals who have died of arsenic poisoning has been found swollen and inflamed, and infiltrated with fluid and the same conditions have been found in animals who have been given lethal doses of arsenic subcutaneously; thus it is considered that these effects are due to the action of the arsenic after absorption and that a similar, but very mild type of effect is at least partly responsible for the **results of therapeutic doses on the alimentary canal.** These are: Increased secretion of saliva and gastric juice, improved digestion and increased appetite, and, after large doses and in poisoning and, in some individuals, even after a few therapeutic doses, nausea, vomiting and diarrhea.

The systemic effects are: Increased permeability of the **capillaries,** which favors the interchange of fluid between the blood and the tissues, this, and other imperfectly understood actions, improves the nutrition of the tissues, including that of the skin and of the bone-marrow, in which blood-cells are formed; the number of **leucocytes** is increased and, sometimes, when the person is anemic, the **red cells.** Poisonous doses cause a rapid destruction of blood-cells. **In pernicious anemia,** which is characterized by excessive destruction of red cells, arsenic tends to lessen the destruction; **in leukemia,** in which there is excessive increase of leucocytes, arsenic restricts their propagation. The cause of these effects in unknown, but it is thought that arsenic may destroy some as yet

undiscovered toxin that, it is believed, induces the abnormal conditions.

Therapeutic Uses.—As a specific in the treatment of syphilis—chiefly salvarsan and neosalvarsan.

As an aid to quinine in the treatment of persistent malaria.

To overcome the infection in some tropical diseases, such as trypanosoma or sleeping sickness.

In pernicious anemia and leukemia.

As a tonic in conditions of debility and poor nutrition.

In the treatment of certain skin diseases.

Arsenic trioxide is occasionally used by dentists, in the form of a paste, to destroy the nerves of teeth.

Toxicology.—Arsenic has been a common cause of poisoning from early time. It was one of the ingredients of the famous *Aqua Tofana* by which so many murders were committed in the sixteenth and seventeenth centuries. At the present time it is one of the drugs most commonly used for committing suicide, for it can be obtained more easily than most poisons as it is the active principle of Paris-green and other vermicides and it is used in a number of industries. Chronic or cumulative poisoning is less common now than formerly, for its causes have been recognized and means taken to prohibit them.

The sources of chronic poisoning are: The dust and vapors arising in industries in which arsenic compounds are used, food, dyes, and the medicinal use of the drug.

Arsenic compounds may be in food because of their use as preservatives or in sprays to protect fruit from attacks of insects, or the employment of arsenic-sulphur compounds (which are very common in nature) to make the sulphuric acid used for preparing glucose from starch. The sulphuric acid is neutralized in the glucose process and, if used with discretion, may do no harm, but, if arsenic impurities are left in the acid, they may cause arsenic poisoning.

How arsenic used in dyes causes poisoning is not fully understood, some chemists believe that particles of the

dye are rubbed off the dyed materal (clothing, paper, etc.) and inhaled, while others think that the dyes are decomposed by certain bacteria which liberate hydrogen from organic matter and that the hydrogen and arsenic combine, forming an exceedingly poisonous gas, *arsenic-hydride*, which is inhaled,

Cumulative poisoning from the medicinal use of arsenic will only occur as the result of carelessness, for there are well marked symptoms of overdosing, but the onset of poisoning from other sources, may be very insidious and the primary symptoms not easily recognized.

The conditions produced by poisonous amounts of arsenic in the body to which the symptoms of accumulative poisoning are due are: Extreme permeability of the capillaries which allows excessive transudation of fluid into the tissues and into the alimentary canal; irritation of the mucous membrane of the alimentary canal, nose, throat, and eyelids; progressive degenerative changes of the tissues, especially those of the liver, spleen, heart, blood-vessels, walls of the stomach and intestines, nervous system, bone-marrow, blood-cells and skin. The blood-vessels are abnormally relaxed and this, together with the condition of the heart muscle and loss of fluid from the blood, causes a great reduction of blood-pressure.

The symptoms of cumulative poisoning vary according to the degree to which the conditions just described are allowed to progress. **In the early stages,** there will be languor and a general feeling of depression; loss of appetite and nausea and, sometimes, vomiting and diarrhea; puffiness under the eyes, due to the excessive amount of fluid exuding from the blood-vessels. The edema shows in this part of the body first because the looseness of the tissue permits of its being easily distended and it is observed chiefly when the person first awakes from sleep, for movement of the muscles dispels the fluid. The edema under the eyes **is the most typical symptom** of the first stages of arsenic poisoning and the one that is most especially to be watched for when patients are

receiving arsenic. **In the more advanced stages,** there will be, in addition to the symptoms just mentioned, redness and itching of the eyelids and conjunctiva; coryza; constant sneezing; hoarseness of the voice; feelings of constriction in the throat and of discomfort in the stomach; anemia; skin rashes, associated with itching of the skin and, sometimes, with areas of discoloration known as *arsenic melanosis;* the hair and, in severe cases, even the nails fall. If the poisoning is not checked, paralysis, especially of the extensor muscles, develops and, consequently, the condition known as *drop-feet* and *drop-wrists;* also, neuritis is common and hypersensitiveness of the joints and skin, and a more or less general edema.

The treatment consists in (1) eliminating the source of poisoning; (2) hastening the excretion of the poison, by the use of non-irritant cathartics and diuretics and of hot baths; (3) treating the injuries that have developed.

The symptoms of acute poisoning may not occur for an hour or more after the ingestion of the drug; they are: Nausea, vomiting, abdominal pain, diarrhea with profuse, watery stools that, after a time, contain shreds of mucous membrane and, therefore, have the appearance described as *rice-water* stools, also, they may contain blood. Thirst is intense, because of the loss of water from the body in the stools. These conditions are soon followed by collapse and sometimes convulsions. The patient may die in a short time, or after two or three days, or may recover and pass through a condition characteristic of cumulative poisoning. If death does not occur at once, the effect of the drug on the kidneys will be shown by the presence of blood and, sometimes, albumin in the urine, and the excretion of urine will be diminished.

Atoxyl, in addition to the above symptoms, causes disturbance of vision, and sometimes, even permanent blindness.

The treatment for acute poisoning consists in washing out the stomach repeatedly (the drug sticks to the inflamed

membrane and is very difficult to remove). If lavage cannot be performed at once, an emetic is given in the interim. One or other of the arsenic antidotes described in the list of iron preparations is usually administered as soon as possible or else a solution of magnesia. Demulcents, such as white of egg and milk, are given liberally and all the fluid possible, for collapse and death are largely due to lack of fluid in the blood-vessels. The usual measures to prevent collapse are employed.

Following the injection of even therapeutic doses of **salvarsan** and **neosalvarsan** some of the following **untoward symptoms** may appear: Headache, giddiness, nausea, vomiting, diarrhea; less commonly, profuse sweating, jaundice, exanthemata, dyspnea, cyanosis, edema, great restlessness, tremors of the muscles, convulsions.

Though some individuals are very easily poisoned by arsenic, others establish a remarkable **tolerance** for the drug and use it indefinitely to improve the complexion and in Styria and the Tyrol the peasants take arsenic compounds habitually because they believe that arsenic keeps them healthy and retards the onset of fatigue during hard labor.

PHOSPHORUS

(Symbol P)

Properties and Distribution in Nature.—Phosphorus is a pale yellowish, translucent, soft solid element. It belongs to the same chemical family as arsenic. It volatilizes readily, giving off fumes that have an odor of garlic, are luminous in the dark and take fire at a very moderate temperature. Phosphorus is only very slightly soluble in water and the body fluids but it is fairly soluble in oils, ether and chloroform. Phosphorus will combine with oxygen and hydrogen in different proportions, thereby forming different acids. It is never found free in nature but its compounds, chiefly salts, are widely distributed, being found in mineral matter, plants and the animal body. **In the body,** calcium phosphate constitutes about 85 per cent. of the mineral matter of the bones and organic phosphorus compounds are essential constituents of other tissues. One of these, known as lecithin, is of particular importance, it occurs in large quantities in the brain and nerves. The body gets its required phosphorus supply from both animal and plant foods, the largest amounts are obtained from milk, eggs, brains, the outer coats of cereals and fruit.

Preparations and dosage:

Phosphorus, $\frac{1}{100}$–$\frac{1}{50}$ gr. (0.0006–0.0012 gm.).

Pills of phosphorus, 1–2 pills. Each pill contains $\frac{1}{100}$ gr. (0.0006 gm.).

Dilute phosphoric acid (10 per cent.), 10–15 m. (0.6–1.0 gm.).

The salts of hypophosphorus acid are known as *hypophosphites*, those commonly used are, calcium, sodium, potassium and iron. The common dosage of all four salts is 15–30 grs. (1.0–2.0 gm.).

Syrup of hypophosphites, 1–2 ʒ (4.0–8.0 gm.). This contains calcium, sodium and potassium hypophosphites.

Compound syrup of hypophosphites, 1–2 ʒ (4.0–8.0 c.c.). *This contains iron hypophosphite as well as calcium, sodium and potassium.*

Salts of glycerophosphoric acid are known as *glycerophosphates.* There are a number of non-official preparations, chiefly syrups, of glycerophosphates in common use.

Calcium glycerophosphate, 2–10 grs. (0.13–0.6 gm.).

Lecithin, 2–10 grs. (0.13–0.6 gm.). *Prepared from yolks of eggs.*

Lecithin solution, 2 per cent. 1 ʒ (4.0 c.c.).

Lecithol, 1 ʒ (4.0 c.c.). *An emulsion prepared from lecithin obtained from the brains of hogs.*

Action and Effects.—If there is a deficiency of phosphorus compounds in the body, the cells may utilize medicinal preparations for their requirements, but phosphorus compounds are so common in food that, unless the individual's supply of food as a whole is deficient, there is not likely to be a lack of phosphorus in the body.

Apart from its power to improve nutrition by supplying a necessary tissue constituent should it be lacking, little is known of the action of phosphorus. **The good effects** that it may induce are: Improvement in the condition of the bones in diseases such as rickets and osteomalacia and, sometimes, in fractures that do not unite readily; increase in the number of red cells of the blood, though not of the hemoglobin. **Bad effects** that will be caused by an excessive amount of phosphorus in the body are: Destruction of bone tissue, especially that of the jaw bones; inflammation and fatty degeneration of the tissues of the organs, especially the liver and the mucous membrane of the stomach and intestines, disintegration of red blood-cells.

The chief therapeutic uses of phosphorus are to obtain its effects on bone and as a tonic in anemia and conditions of malnutrition.

Toxicology.—Acute poisoning is usually the result of attempt to commit suicide with phosphorus compounds

intended for the destruction of vermin and **chronic poisoning** by the inhalation of phosphorus fumes, when employed in industries, especially match-making, in which phosphorus is used. Chronic poisoning is less common now than formerly, because it is illegal to use untreated yellow phosphorus for matches and its substitutes are less poisonous.

The symptoms of acute poisoning may not appear for several hours after the drug is swallowed. They are abdominal pain, nausea, vomiting and diarrhea. The vomitus and stools will have an odor of garlic and emit light in the dark, later they may contain blood and hemorrhages may occur from the nose, throat, uterus, and under the skin. There will be the usual symptoms of shock and there may be convulsions and delirium.

The treatment consists in lavaging the stomach; giving copper sulphate (which acts both as an emetic and a chemical antidote) permanganate of potash (which tends to oxidize the phosphorus) and demulcents such as milk and white of egg, but not oils, for oil by increasing the solubility of phosphorus, hastens its absorption. Later alkaline solutions are given to lessen the acidosis caused by the abnormal metabolism.

The symptoms of chronic poisoning are: Caries of the teeth, lesions of the gums and, in advanced cases, necrosis of the jaw bones and fragility of other bones; a tendency to diarrhea, indigestion, and bronchitis; anemia; cachexia; jaundice (due to interference with the discharge of bile from the ducts by the condition of the liver); and there may be albumin in the urine.

The treatment consists in eliminating the cause and treating the abnormal conditions by the usual methods.

ANTIMONY

(Symbol Sb)

Antimony is a bluish-white metallic-like element that exists in many minerals. It belongs to the same chemical family as arsenic and phosphorus. The official preparations are those of a salt formed by the action of antimony oxide on cream of tartar.

Preparations and dosage:

Antimony and potassium tartrate (tartar emetic), 1/30–1/15 gr. (0.002–0.004 gm.) or, as an emetic, 1/2–2 grs. (0.03–0.13 gm.).

Compound syrup of squill, 5–30 m. (0.3–2.0 c.c.). *This contains tartar emetic* 2 *per cent. and fluidextracts of squill and senega, a.a.* 8 *per cent.*

Wine of antimony, 5–30 m. (0.3–2.0 c.c.) or, as an emetic, 1–2 ʒ (4.0–8.0 c.c.). *This contains* 10 *per cent. tartar emetic.*

Antimony lithium tartrate (non-official), 1/2–3 grs. (0.03–0.2 gm.).

Fate in the Body.—Antimony is absorbed, though not very readily, through the skin and mucous membranes; it is taken up by the tissues in the same way as arsenic, but much more slowly; it is excreted through the kidneys and, even when given intravenously, the stomach and intestines.

Action and Effects.—The action of antimony is similar to that of arsenic, but it is more irritant. Like arsenic it has a particularly destructive effect upon the higher types of microörganisms such as spirochæta and protozoa.

Applied to the skin, dilute solutions act as rubefacients and strong ones produce blisters and pustules and even ulceration. If given hypodermically, it causes intense pain and tends to promote suppuration.

Antimony is so irritant to **mucous membranes** that even in small doses it causes nausea. This effect is more pronounced when the drug is taken by mouth but, as the alimentary canal is irritated by the portion excreted through it, nausea is likely to follow any method of administration. Comparatively large doses cause vomiting and diarrhea.

The secretions of saliva, bronchial mucus, and perspiration are increased, but this is the result of the nauseant action and is not due to a direct stimulation of the glands by the drug.

Antimony tends to relax the **blood-vessels** and to depress the **heart** action, but, in therapeutic doses, this depression is due to the nauseant action.

Therapeutic Uses.—Because of its untoward effects antimony is little used in therapeutics except in small doses as an expectorant or, occasionally, as a diaphoretic, and, intravenously, to destroy organisms causing some tropical diseases such as trypanosomiasis or sleeping sickness.

Toxicology.—Poisonous doses produce such intense irritation of the alimentary tract that very little of the drug is absorbed and thus the **symptoms** are almost entirely due to the irritation of the alimentary canal. They are: Extreme nausea; vomiting; profuse watery diarrhea similar to that of arsenic poisoning; excessive perspiration; and the usual symptoms of collapse.

The special points in the treatment are: To give lavage, even though vomiting is so profuse, because the drug tends to adhere to the inflamed membrane; to give all the fluid possible both to replace the water lost from the system and to minimize the irritation of the kidneys by any of the drug that is absorbed and to give demulcent beverages to allay the irritation of the alimentary membrane.

IODINE (IODUM) AND ITS COMPOUNDS

(Symbol I)

Iodine is a purplish-black solid element which crystallizes in brilliant plates and, even at ordinary temperatures, gives off a beautiful violet vapor to which its name is due, the term iodine being derived from a Greek word meaning violet. **Iodine is found** combined with other elements in the ashes of certain sea plants, in Chili saltpeter and in salt springs. **It combines** readily with a number of elements and compounds. In combination with hydrogen it forms hydriodic acid and this combines with alkaline substances to form salts—iodides.

Preparations and dosage:

Tincture of iodine, 3–8 m. (0.2–0.5 c.c.). *This is an alcoholic solution of iodine 7 per cent., and potassium iodide 5 per cent.*

Compound tincture of iodine (Lugol's solution), 5–10 m. (0.3–0.6 c.c.). *This consists of iodine 5 per cent. in a 10 per cent. solution of potassium iodide.*

Hydriodic acid, (10 per cent.), 5–10 m. (0.3–0.5 c.c.).

Potassium iodide (KI), 5–20 grs. (0.3–1.3 gm.).

Sodium iodide, 5–20 grs. (0.3–1.3 gm.).

Iodoform, 1–3 grs. (0.06–0.2 gm.).

New and non-official preparations:

Iodipin, 5–10 grs. (0.3–0.6 gm.).

Iodipin solution, 10 per cent., 1–2ʒ (4.0–8.0 c.c.).

Iodipin solution, 25 per cent. ½–3ʒ (2.0–4.0 c.c.).

Iodival, 10, 30 grs. (0.6, 2.0 gm.).

Sajodin, 10–30 grs. (0.6–2.0 gm.).

The above are iodized fats.

Iodol, 2–4 grs. (0.13–0.25 gm.). *This is obtained by the action of iodine on mineral oils.*

Iodalbin, 5–10 grs. (0.3–0.6 gm.). } Iodized
Iodocasein, 5–20 grs. (0.3–1.3 gm.). } proteins

There are also a number of new preparations for external use, the most important of which are: Aristol (or thymol iodide); iocamphen (iodine, phenol and camphor); and vioform.

Administration.—Tincture of iodine, hydriodic acid and the alkaline iodides must be well diluted for internal administration. The iodides are generally given in milk or a flavored diluent that will disguise their taste. The tincture of iodine is best given in a glass (6 ounces) of milk. When used externally, the tincture of iodine must not be applied while the skin is moist because moisture hinders the absorption of the iodine and makes it more irritant.

Fate in the Body.—The tincture of iodine and other preparations for internal use are readily absorbed from mucous membranes; the tincture is also absorbed to a slight extent through the skin, and this and other compounds may be absorbed from wounds. Iodine and the iodides are excreted readily, traces being found in the urine and saliva, under normal conditions, a few minutes after the ingestion of the drugs and from 60 to 80 per cent. of a dose will have left the body within 24 hours. The organic combinations, especially the fat compounds are not excreted as quickly as the others. They are decomposed in the body with the liberation of iodides. All of these drugs are excreted chiefly through the kidneys, but also in the saliva, secretions of mucous membrane and, when the mammary glands are active, in the milk. While in the body they are retained chiefly in the blood, thyroid gland and in abnormal tissues such as those which form around tubercular organisms and the spirochæta of syphilis that invade the body. Iodine is a normal constituent of the thyroid secretion and thus its absorption by this gland is easily understood. The passage of iodine compounds into abnormal tissue to a greater extent than normal is thought to be due to lack of normal resistance

to the penetration of salts by the poorly nourished cells of abnormal tissue.

Actions.—**Iodine** combines readily with protein and other constituents of protoplasm and, thereby, except in very dilute solutions, it contracts and hardens tissue and acts as an irritant. It discolors anything with which it comes in contact, but the discoloration can be easily removed by washing the stain with soap and water, or ammonia, or alcohol. **The iodides** do not combine with the elements of protoplasm, but they have a salt action and thus act as irritants to the soft tissues. The **organic preparations** are less irritant than the inorganic iodides.

All the preparations for internal use after absorption, owe their chief therapeutic effects to their iodine. The exact nature of the iodine action after absorption (when it is much diluted) is not known but its effects are thought to be due chiefly to stimulation of the thyroid gland and the disintegration of abnormal connective tissue. Also it tends to lessen the viscosity of the blood.

Effects of Actions—On Bacteria.—Iodine is an excellent germicide. The tincture has been found to destroy even streptococci and gonococci within one minute. It is a particularly good disinfectant for the skin as, even in dilute solutions—2–3 per cent.—it will destroy the staphylococci commonly present on the skin within a minute or two. Also, unlike most disinfectants, iodine tends to penetrate the outer layer of skin to some extent.

Iodoform has a slight antiseptic action when in contact with wounds, for the secretions of the wound decompose it and liberate iodine to which its action upon microörganisms is due. **Most of the other compounds for external use** contain phenols or similar substances which may possibly increase their antiseptic action. However, all of these preparations, including iodoform, owe most of their antiseptic value to their power of absorbing wound secretions and thus rendering the surface of the wound dry and unsuitable for the life of bacteria.

When applied to the skin, tincture of iodine acts as a

counterirritant. Its irritant action is less severe, but more prolonged, than that of most of the drugs used as counterirritants. Concentrated solutions, however, will cause blistering and even corrosion if used in excess, especially if the part to which the application is made is moist or if it is covered, so that the evaporation of the iodine is prevented. **The other iodine compounds** are not irritant to the skin in their natural state, but, if iodoform is used on wounds in excessive amounts, the iodine liberated may cause irritation and a consequent dermatitis. Also, **skin eruptions** of various types are likely to follow the internal use of, especially, the alkaline iodides. The reason for this is not known, it was formerly thought the eruptions were the result of irritation of the skin glands during elimination, but such a small amount is excreted through these glands that the idea has been abandoned.

By their irritant action on mucous membranes iodine and the iodides increase the secretion of saliva, gastric juice and respiratory and alimentary mucus and they tend to fluidify the mucus and to make it less tenacious. As previously stated, iodine compounds are excreted to some extent in the saliva and, when they are taken for some time, they are likely to induce salivation, and swelling and congestion of the throat, tonsils and gums, and to be the cause of a persistent, disagreeable taste. These effects are more readily induced by the alkaline iodides than other preparations. The tincture of iodine and, though to a lesser degree, the alkaline iodides are very irritating to the stomach and intestines and, unless properly diluted, they will cause nausea, vomiting and sometimes diarrhea.

After absorption, iodine, in whatever form it is used, tends to improve **nutrition.** This effect is thought to be due chiefly to the stimulation of the thyroid gland, the secretion of which is essential for metabolism. Iodine has little effect upon the **circulation** when the blood and circulatory organs are normal, but it tends to reduce abnormally high blood-pressure under some conditions

by, it is thought, increasing thyroid activity, lessening the viscosity of the blood and, improving the condition of sclerotic blood-vessels when this is due to syphilis. As the result of its effects upon the abnormal tissue (gumma) that forms in various parts of the body, under the influence of the organism that causes syphilis, iodine tends to relieve many of the pathological conditions occurring in the tertiary stages of that disease. The relief is thought to be due to at least two factors: (1) The removal of abnormal tissue which is interfering with the functioning of organs; (2) the disintegration of the gummata in which the spirochæta are encased for they can then be destroyed by the syphilitic specifics mercury and arsenic.

Iodine has the same **effect upon the tubercles that form around the tubercle bacilli** when they invade the body that it has on the gumma of syphilis, but, as there is no known specific germicide for the tubercle bacilli, most investigators consider iodine a dangerous drug to use when a person has tuberculosis, since, when the organisms are set free by the disintegration of the tubercles, they may invade fresh tissue. Some physicians, however, believe that iodine tends to destroy the bacilli and that good effects may be obtained if the drug is used with caution. When it is used, special care must be observed to note and record all symptoms that arise.

The secretion of urine is slightly increased by iodides for the same reason that it is by other salts.

The Principal Therapeutic Uses.—Iodine is employed chiefly as a disinfectant for the skin, mucous membranes and wounds, and it is occasionally substituted for the iodides.

Iodoform and similar preparations are used as antiseptics on ulcers and sores of like nature and, occasionally, in wounds.

The iodides and other preparations for internal use are employed: In the tertiary stage of syphilis; in arteriosclerosis and some other conditions characterized by excessive

connective tissue formation; and the iodides are common ingredients of expectorant mixtures.

Toxicology:

The symptoms of acute poisoning by iodine are those of irritant drugs, with particularly marked symptoms of collapse, and the vomitus will turn blue if starch paste is added to it. **The treatment** is the same as for poisoning by other irritants and, in addition, a starch paste is given, for the starch unites with the iodine to form a relatively harmless iodide of starch.

Iodoform poisoning is usually the result from the absorption of the drug from wounds. **The symptoms** of poisoning vary considerably. Most of them are thought to be due to the action of the iodoform on nerve-centers and to increased thyroid activity. In mild degrees of poisoning there is likely to be a taste of iodoform in the mouth; headache; dizziness; loss of appetite; restlessness; sleeplessness and mental depression. The pulse becomes accelerated and there may be a rise of temperature. If the intoxication is allowed to proceed, the nerve depression will deepen into melancholy or, sometimes, delirium, followed in severe poisoning, by coma and collapse.

Chronic poisoning, known as *iodism,* is very likely to occur, unless care is taken, when iodine compounds are used in the treatment of syphilis, because, to be effectual, they must, as a rule, be taken for at least three years.

The symptoms are: Skin lesions, which, unless care is taken, may become very serious; congestion of the conjunctiva with excessive secretion of tears; salivation; congestion and swelling of the mucous membrane of the nose and throat with inordinate secretion of mucus and frequent attacks of sneezing. The congestion may extend to the frontal sinuses and give rise to intense headache. There may be nausea and vomiting and, sometimes, diarrhea. In severe cases there are likely to be emaciation, tachycardia (rapid heart action) and extreme nervousness due, it is thought, to abnormal activity of the thyroid gland.

In order to prevent iodism the first appearance of symptoms should be reported to the doctor and the skin and mouth must be kept particularly clean. Why frequent bathing tends to retard the onset of an eruption is not known, because, as previously stated, the drugs are not eliminated to any extent through the skin. The throat should be gargled with a cleansing fluid, such as a solution of sodium bicarbonate, at least three times a day.

IPECAC (IPECACUANHA) EMETINE

Ipecac is prepared from the roots of the *Cephaëlis Ipecacuanha* and similar species of trees. It contains three alkaloids, the principal one of which is emetine.

Preparations and dosage:

Ipecac, expectorant dose, 1 gr. (0.06 gm.).

Ipecac, emetic dose, 15 grs. (1.0 gm.).

Ipecac, in dysentery, 30–50 grs. (2–4 gm.).

Fluidextract, expectorant dose, 1 m. (0.06 c.c.).

Fluidextract, emetic dose, 15 m. (1.0 c.c.).

Syrup, expectorant dose, 15 m. (1.0 c.c.).

Syrup, emetic dose, 4ʒ (16.0 c.c.).

Wine, expectorant dose, 10–30 m. (0.6–2.0 c.c.).

Wine, emetic dose, 4 (16.0 c.c.).

Dover's powder, 5–15 grs. (0.3–1.0 gm.). *A powder of 10 grs. contains 1 gr. each of ipecac and opium and 8 grs. of sugar of milk.*

Emetine hydrochloride in amœbic dysentery, ½ gr. (0.03 gm.). Emetic dose, ½–1 gr. (0.03–0.06 gm.).

Emetine-bismuth-iodide, 3–4 grs. (0.2–0.25 gm.).

Administration.—The large doses of ipecac used in the treatment of dysentery are given either in keratin capsules, salol coated pills or in solution through a duodenal tube, as described on page 290. The salol and keratin are not readily dissolved by the gastric juice and thus the ipecac is not set free until it reaches the intestines where, in dysentery, its action is required. Emetine hydrochloride is given by hypodermic when it is used in amœbic dysentery, for, if given by mouth, it is likely to cause vomiting and then enough of the drug will not reach the intestine to be of use, but the emetine-bismuth-iodide preparation is given by mouth because it is insoluble in the acid gastric juice and only becomes active when it is dissolved by the intestinal juice.

Fate in the Body.—Even when given by hypodermic, emetine is excreted chiefly through the intestines, but to some extent through the kidneys.

Actions and Effects.—Ipecac and its active principle emetine owe their value to their local irritant action and to their specific poisonous action on the amœba that cause dysentery. They are not used for their actions after absorption and these are not well understood, but it is believed that they may add to the general depression that occurs in poisoning.

These drugs have a bitter acrid **taste** and, when taken by mouth, they induce a copious flow of saliva. They are very irritant to **mucous membrane** and therefore a small dose taken by mouth will induce a prolonged nausea with the conditions that practically always attend nausea, viz., increased secretion of saliva and bronchial and alimentary mucus, increased perspiration, sensations of weakness and depression, and a relatively rapid and weak pulse. Emetic doses will, as a rule, induce vomiting in a few minutes and the conditions just mentioned will be intensified. Emetine, if given in doses above 1 grain by hypodermic will cause vomiting and it was formerly thought that it did so by stimulating the vomiting center, but it is now believed that this may be due to its irritant action in the stomach and intestine during excretion. It is because so much of the drug is excreted through the intestinal wall that it affects the amœba when given by hypodermic.

The therapeutic uses of ipecac are: (1) To increase and fluidify bronchial mucus, *i.e.*, to act as an expectorant; (2) to induce vomiting, *i.e.*, to act as an emetic; (3) to increase perspiration, *i.e.*, to act as a diaphoretic, for this purpose it is employed chiefly to overcome conditions conducive to colds, see page 342, and it is the Dover's powder that is generally used; (4) to destroy the amœba that causes amœbic dysentery, for which it is a specific.

The symptoms of poisoning and the **treatment** are those of irritant drugs.

CINCHONA AND QUININE

Cinchona is obtained from the bark of certain species of trees—the *cinchona*—which grow in several tropical countries, but especially those of the northern part of South America. It was so called after the Countess of Cinchon—a Spaniard whose husband was governor of Peru—because its first recorded use was for the countess, in 1638. Knowledge of its curative effects in the disease then known as *ague*, but now termed *malaria*, was obtained by the Spaniards from the Peruvian Indians.

Cinchona contains about nineteen alkaloids, of which the principal one is quinine. The others have about the same action as quinine, but are less powerful. Thus the actions of cinchona and the preparations of other alkaloids are similar to those of quinine, but weaker.

Preparations and dosage:

Fluidextract of cinchona, 15–30 m. (1.0–2.0 c.c.).

Tincture of cinchona (20 per cent.), 1–2ʒ (4.0–8.0 c.c.).

Compound tincture of cinchona (10 per cent., with bitter orange peel and serpentaria), ½–1ʒ (2.0–4.0 c.c.).

Quinine, 5–15 grs. (0.3–1.0 gm.).

Quinine bisulphate, 5–15 grs. (0.3–1.0 gm.).

Quinine sulphate, 5–15 grs. (0.3–1.0 gm.).

Quinine hydrobromide, 5–15 grs. (0.3–1.0 gm.).

Quinine hydrochloride, 5–15 grs. (0.3–1.0 gm.).

When only one dose of the above quinine salts is given per day, in the treatment of malaria, larger doses, usually about 30–40 grs. (2.0–2.6 gm.) are sometimes prescribed.

Iron and quinine citrate, 5–10 grs. (0.3–0.6 gm.).

Syrup of iron, quinine and strychnine phosphate, ½–1ʒ (2.0–4.0 c.c.).

Elixir of iron, quinine and strychnine phosphate, ½–1ʒ (2.0–4.0 c.c.).

Warburg's tincture (*this contains quinine, a number of volatile oils, opium and aloes*), ½–1ʒ (2.0–4.0 c.c.).

Cinchonine sulphate (*an alkaloid of cinchona*), 5–20 grs. (0.3–1.3 gm.).

Cinchonidine sulphate (*an alkaloid of cinchona*), 5–20 grs. (0.3–1.3 gm.).

Non-official compounds and derivatives of quinine:

Chinaphenin (*quinine and phenacetine*), 5–10 grs. (0.3–0.6 gm.).

Saloquinine (*quinine and salicylic acid*), 10–30 grs. (0.6–2.0 gm.).

Saloquinine salicylate (*quinine and salicylic acid*), 15 grs. (1.0 gm.).

Quinine tannate, 10–30 grs. (0.6–2.0 gm.).

Quinine and urea chloride, 5–15 grs. (0.3–1.0 gm.).

Aristochin (*prepared from quinine*), 5–15 grs. (0.3–1.0 gm.).

Euquinine (*prepared from quinine*), 5–15 grs. (0.3–1.0 gm.).

Optochin (*this is prepared from hydroquinine and also an alkaloid cupreine, which is obtained from the China cuprea bark. It resembles quinine.* 5 grs. (0.3 gm.).

Administration.—When used for its bitter effect, quinine is given before meals. As a rule, cinchona or only very small doses of quinine are prescribed for this purpose and nothing must be done to disguise the taste. When quinine is used in the treatment of malaria, either one of the three following methods of administration is commonly used. (1) One large dose is given about three hours before the time of the chill[1] so that the quinine will be in the

[1] It will be remembered that when the organisms which cause malaria are injected into the blood by an infected mosquito they enter red blood-corpuscles, where they grow, multiply and, finally, cause the rupture of the corpuscles in which they have been harbored. Unless the parasites are killed while they are free in the blood, they enter new cells and the cycle is repeated. It is while the organisms are free in the blood that the malarial chill occurs. The length of time that the parasites take to develop and thus the length of the interval between chills depends upon the type of organism causing the infection, but it is the same for each species and thus after the two first chills the hour at which subsequent ones will occur can usually be foretold.

blood when the malarial organisms break free from the corpuscles. (2) The total amount is given in divided doses the first one about six hours before the expected chill, and the last one just about the time that the chill usually occurs. (3) The total amount is given in divided doses at intervals during the time that the temperature is falling after the chill. When not used for the above purposes quinine is given after meals because the presence of food lessens its irritant action on mucous membrane and, also quinine sulphate is not very soluble, except in an acid medium, and the gastric fluid is normally, only acid during digestion. For this reason, when the quinine is given at other times, if it is not already in a prepared solution, a drop of dilute sulphuric acid is given with it and it should be given in or with something that will disguise its bitterness.[1] For rectal irrigations, urea chloride is diluted to about 0.5 per cent. and other preparations to between 1:3000–1:500.

Fate in the Body.—Quinine is readily absorbed from the stomach if the gastric contents are acid, otherwise its solution and, consequently, its absorption are slow and imperfect. After absorption a very considerable portion of each dose is thought to be destroyed in the tissues for only about ⅓–½ of a dose is eliminated. Elimination takes place chiefly through the kidneys, but traces are occasionally found in the perspiration, bile and milk. The greater part of a dose will be excreted within 8 or 10 hours.

Action.—Quinine is a general protoplasmic poison. It first stimulates and then depresses the protoplasm of almost all tissues. However, it affects some tissues more readily than others and, though some tissues are markedly stimulated and not readily depressed, others may be depressed with little or no evidence of primary stimulation.

The protoplasm of microörganisms exhibits the same

[1] A drug named Eriodictyon or *Yerba Santa* which lessens the appreciation of bitter flavors is often used for this purpose. The dose of the fluidextract is 15–60 m. (1.0–4.0 c.c.).

difference in sensitiveness to the action of quinine as animal tissue and thus some forms, especially the protozoa, are more readily destroyed than others.

The skin may be very slightly irritated by local applications of quinine.

Mucous membranes, subcutaneous tissues and pain nerve-endings are first irritated and then, especially the nerve-endings, depressed upon contact with the drug.

When quinine is taken by mouth the taste-buds which respond to bitter are stimulated and the action of the **ferments** which digest proteins are depressed.

After its absorption quinine affects chiefly:

1. **The Blood and Ferments.**—It depresses the white corpuscles; it inhibits the action of the ferment concerned in the coagulation of blood and that which promotes oxidation and probably other ferments that stimulate catabolism.

2. **Muscle Tissue.**—The skeletal muscles, cardiac muscle and the plain muscle tissue of the blood-vessels, bronchi, spleen, and uterus are particularly influenced, being slightly stimulated by moderate doses, but depressed by large ones. The effects on the muscle of the blood-vessels in the inner ears and eyes are especially marked.

3. **Nerve Tissue.**—Some part of the sensory mechanism that responds to pain is apparently slightly depressed. Otherwise, therapeutic doses do not seem to affect the nervous system, but poisonous doses will, after a temporary stimulation, depress nerve centers, especially medullary centers, and death is usually the result of paralysis of the respiratory center. The ganglia in the cochlea of the inner ear and the retinal nerve-cells may be destroyed by large doses. Formerly it was thought that the heat regulating center was stimulated but experiments have shown that this is not the case.

Effects of Actions On Microörganisms.—Quinine, even in dilute solutions—1:500—will retard the activity of bacteria, but its destructive action is more marked on protozoa, such as the malarial organisms and the amœba, and the malarial

organisms are more easily destroyed if the quinine reaches them while they are free in the blood plasma.

On the skin, the only effect of local applications is a slight increase in the amount of blood at the area of application, especially if this is the scalp and, in such case, the increased blood supply may favor the growth of hair. A skin rash often follows the continued use of quinine and it is thought that this may be partly due to irritation of the skin by the quinine that is eliminated in the perspiration.

When quinine is **injected subcutaneously** it causes pain, but, when the preparation quinine and urea chloride is used, the irritation is followed by a local anesthesia that may persist for some hours.

When quinine is **taken by mouth** it acts as a bitter and thereby tends to improve the appetite and increase the secretion of saliva and gastric juice but, nevertheless, unless the dose is small and well diluted, the digestion of proteins is inhibited, because of the inactivity of the ferments. For this reason, cinchona, which is equally bitter, but less destructive to the ferments is more commonly used as a bitter than quinine. Large doses of either drug, but especially quinine, will cause nausea and vomiting.

Effects of Moderate Doses after Absorption.—If there are **malarial organisms** in the blood, they will be destroyed. The power of the **blood to coagulate** is lessened. The number and the activity of the **leucocytes** is diminished; this is a very undesirable effect in infections due to pyogenic bacteria and in other diseases in which leucocytosis is depended upon for the body's protection.

Blood-pressure is slightly raised and the pulse tends to become somewhat accelerated. Thus the circulation in most parts of the body is improved. Occasionally, however, the effect of even moderate doses upon the muscle tissue in blood-vessels of the cerebrum, ears and eyes may interfere with the circulation in these organs and, by causing either anemia or congestion, give rise to the symptoms described under Cinchonism. The interference with

the circulation is also partly responsible for the degeneration of the nerve-cells in the cochlea and retina that sometimes occur in poisoning.

The action of quinine (in moderate doses) on skeletal muscles, tends to increase their power, but the muscles are soon fatigued. As a rule anything which increases muscular contraction, increases catabolism but, for some undiscovered reason, after a very transitory increase, the catabolism of proteins is reduced. As the primary stages of catabolism are inhibited there is not, as is usually the case when drugs interfere with metabolism, an accumulation of waste products in the system, but a storing of protein, which aids body nutrition in conditions, such as fever, when there is a tendency to abnormal destruction.

Unless quinine is taken in large doses it does not affect the normal **temperature** but moderate doses tend to reduce fever. The reason for the influence of quinine upon the temperature is uncertain; some investigators consider that it is due to the lessened destruction of proteins but others believe that the quinine acts by lessening the vitality of the organisms causing the fever.

Quinine reduces the size of the **spleen** by contracting its muscle tissue.

If quinine is taken during **pregnancy** it may cause abortion, and, if taken during **labor**, it increases the strength of the uterine contractions.

Quinine has some power to relieve mild **pain**, especially that occurring in connection with colds, influenza and neuralgia.

A moderate increase in the secretion of **urine** may follow therapeutic doses of quinine, due, to irritation of the kidney, but this action is only pronounced when large doses are taken and, in such case, there may be albumin and even blood in the urine.

Therapeutic uses of quinine are.—As a gargle, to contract the throat tissue when it is relaxed.

In solutions used for irrigations to overcome gonococci infection or to rid the intestine of pin-worms or to destroy amœba causing dysentery.

In hair tonics, to stimulate the growth of hair.

For its bitter effects, but, for reason already given, cinchona is more commonly employed for this purpose.

Quinine and urea chloride or, sometimes, quinine bisulphate is used as a local anesthetic. The former is also injected around hemorrhoids, or used in suppositories, to lessen pain and to reduce the size of the enlarged veins. Also, it is sometimes injected into enlarged thyroid glands in large enough doses (about twice the usual dose) to destroy some secretory cells.

For its effects after absorption, quinine is used: To destroy the malarial organism. To improve nutrition when there has been loss of flesh. As an ecbolic (to hasten parturition) in the second stage of labor. To check profuse menstruation. To lessen pain and reduce the temperature in influenza and similar affections. To cause contraction of the spleen in diseases associated with its enlargement.

Optochin has a particularly destructive effect upon the pneumococci and is therefore used in pneumonia.

Toxicology:

Cinchonism is the term applied to certain of the symptoms that quinine induces when it is taken in large doses or when it is taken in smaller doses for a considerable time. Occasionally, due to idiosyncrasy, even one moderate dose may induce some of the symptoms. These are: Ringing in the ears and partial deafness; less commonly, disturbance of vision, especially for colors; headache; dizziness; and mental dullness; (these symptoms are thought to be due chiefly to interference with the circulation in the cerebrum, ears and eyes); muscular weakness; a slow, weak pulse due to depression of the heart muscle. Associated with cinchonism there may be skin eruptions (due, it is thought, to interference with the circulation in the skin and to irritation of the skin by the drug in the perspiration); nausea; vomiting; diarrhea.

The treatment for cinchonism consists in discontinuing the use of the drug and giving bromides or analgesics such

as phenacetine. These drugs are often prescribed with quinine for susceptible individuals.

If a poisonous dose is taken the symptoms just mentioned will be very pronounced and deafness or blindness may be complete and, if the nerve-cells are destroyed, permanent. Also, the breathing becomes slow and shallow and collapse is likely to occur. Death, however, is not a common outcome; when it does occur, it is nearly always due to paralysis of the respiratory center with consequent failure of breathing.

The treatment is the same as for cinchonism, plus lavage, the usual means to avert collapse and, if necessary, artificial respiration.

SALICYLIC ACID, SALICYLATES

Salicylic acid is a white crystalline powder. It occurs in nature in combination with certain volatile oils, chiefly those existing in wintergreen (*gaultheria procumbens*) and birch bark (*Betula lenta*), also it is prepared synthetically from phenol (carbolic acid) with sodium hydroxide and carbonic acid.

The inorganic salicylates are salts of salicylic acid and the alkaline substance in each salt is indicated by the name of the latter. There are also **organic salts,** and other combinations of salicylic acid some of which are obtained from the volatile oils just mentioned and others are **synthetical products.** Some of the latter are prepared from coal tar products, but they liberate salicylic acid when they are decomposed in the body and thus have about the same, but milder, action as the acid and the inorganic salicylates.

Preparations and dosage:

Salicylic acid, 5–30 grs. (0.3—2.0 gms.).
Ammonium salicylate, 3–6 grs. (0.2–0.4 gms.).
Lithium salicylate, 5–20 grs. (0.3–1.3 gms.).
Sodium salicylate, 5–30 grs. 0.3–2.0 gms.).
Strontium salicylate, 15 grs. (1.0 gm.).
Oil of wintergreen, (*Oleum gaultheriæ*), 5–15 m. (0.3–1.0).
Oil of sweet birch, (*Oleum betula*), 5–15 m. (0.3–1.0).
Methyl salicylate, 5–15 m. (0.3–1.0).
Ethyl salicylate (not official), 5–15 m. (0.3–1.0).
Salicin, 5–30 grs. (0.3–2.0 gms.).
Salol, 5–30 grs. (0.3–2.0 gms.).

Non-official preparations:

Aspirin (Acetylsalicylicum), 5–15 grs. (0.3–1.0 gm.).
Novaspirin, 5–15 grs. (0.3–1.0 gm.).

Diaspirin, 5–15 grs. (0.3–1.0 gm.).
Salophen, 5–15 grs. (0.3–1.0 gm.).
Saloquinine salicylate, 5–15 grs. (0.3–1.0 gm.).
Lactophenine, 8–15 grs. (0.5–1.0 gm.).
Malakine, 8–15 grs. (0.5–1.0 gm.).
Neurodine, 8–15 grs. (0.5–1.0 gm.).

For external use:

Thiersch powder, *this consists of boric acid and salicylic acid., a. a.* ℥ 1. *In preparation for use a powder is dissolved in, usually,* 1 *quart* (1000 *c.c.*) *of boiling water.*

Salicylic ointment.

Salicylic acid is also one of the most common ingredients of the plasters and collodions used as corn cures.

Mesotan, *this is a methyl ester of salicylic acid, it is diluted with an equal amount of olive oil in preparation for use.*

Spirosal, *this also is an ester of salicylic acid. It is dissolved in either* 3 *parts of alcohol or* 6–8 *parts of oil in preparation for use.*

The oil of wintergreen and oil of birch are used externally as well as internally.

In addition to the salicylates here mentioned there are some which do not owe their chief effects to the salicylic ion. These are classified with the drugs whose action they resemble.

Administration.—For oral administration the drugs of this series are best given in capsules. If capsules are not to be had, the acid and the volatile oils should be mixed with syrup.

Sodium bicarbonate is often prescribed with the salicylates in order to, by lessening the acidity of the gastric juice, inhibit the decomposition of the salts and the consequent liberation of the acid, which is much more irritating to the mucous membranes.

When a salicylate is given hypodermically, a local anesthetic is generally injected first to prevent pain, and the salicylate must be diluted to at least 20 per cent.

Sodium salicylate is sometimes given in relatively large

doses (up to 2 drams once a day) by rectum. The usual technique of this method of administration is as follows: A soap-suds enema is given about an hour previous to the administration of the salicylate. The latter is dissolved in about 6 ounces of water and 15 minims (1.0 c.c.) of opium are added. The enema is administered in the usual manner of giving enemata that are to be retained.

Fate in the Body.—The volatile oils methyl and ethyl salicylates, mesotan, and spirosal are absorbed to some extent through the skin, but the other preparations are not. They are, however, readily absorbed from the stomach and intestines. After absorption they are retained in the tissues for some time and they are taken up by the cells of synovial membranes, and are found in the synovial fluid aspirated from joints. Also they seem to pass into many types of inflammatory processes, when such exist, for they are found in most inflammatory exudates. They are excreted chiefly by the kidneys in the form of salicyluric acid, but they are also eliminated in the perspiration, bile and milk. Their excretion is slow.

Actions.—The drugs of this group depend upon the acid (salicylic) ion for their actions and thus these are similar. The inorganic salicylates, however, are less irritating than the acid and the volatile oils and most of the new preparations are less irritating, but also less powerful, than the inorganic salts.

Beyond, that it is irritating to most tissues, and destructive to microörganisms, so little definite information could be found of the ways in which salicylic acid produces its chief effects that its actions will not be described separately.

Effects.—Salicylic acid and, though to a less extent, the salicylates are antiseptic. Salicylic acid in strengths as dilute as 1: 500 will retard the growth of bacteria, moulds and yeasts.

On the skin, methyl and ethyl salicylates, the volatile oils of wintergreen and birch, and mesotan act as counter-

irritants and in concentrated preparations, especially if their evaporation is prevented, they may cause corrosion. Powdered salicylic acid is also irritant to the skin but when it is combined with substances such as oil or collodion or when in solution it is only slightly so and it tends to soften hardened epithelium, such as corns, and to lessen inflammatory conditions such as occur in many skin diseases. Also, it checks local sweating, as of the feet, by a local action upon either the secretory cells or nerve-endings of the sweat glands. As will be seen later this is the opposite effect of its action after absorption. The other preparations of the group have no effect upon the skin.

The most valuable effects of salicylic acid after absorption are: (1) It tends to relieve the pain and cure the conditions in joints affected by **acute articular rheumatism.** Some investigators consider that this is the result of a specific action on the microörganisms causing the disease, but others believe that the acid acts, not upon the organisms, but upon their toxins, either causing their destruction or hastening their elimination. (2) It may relieve pain due to **gout** and to some of the **chronic affections** commonly spoken of as rheumatism, but it does not cure such conditions. (3) It is analgesic in **neuritis.** (4) It induces free **perspiration** and **dilation** of the superficial blood-vessels and, by these means, even though it stimulates catabolism, it reduces the **temperature** when there is fever, but not otherwise, unless it is taken in large doses. The diaphoresis and increased amount of blood at the surface of the body also tends to lessen congestions that are the forerunners of **colds,** and in this way, will often avert a cold if taken in the early stages. (5) Salicylic acid tends to promote the **absorption of effusions,** but how it does so is not known for, though it has a slight diuretic action, this is not sufficient to remove enough fluid from the blood to favor as much absorption as sometimes occurs. The **diuresis** is supposed to result from a mild irritation of the kidneys and the increased amount of urea which is

in the blood as the result of the augmented catabolism of proteins. (6) Salicylic acid acts as an antiseptic in the urinary tract. (7) It increases the excretion of uric acid.

The **heart muscle** and the **vasoconstrictor** and **respiratory centers** may be slightly stimulated by small doses, but they are depressed by large doses and, occasionally, even moderate doses will have this effect in some individuals. Thus the **pulse** is likely to be somewhat stronger and faster after moderate doses, but slow and weak after large doses; and the rate of **breathing** may be slightly increased after moderate doses, but dyspneic after large doses.

Large doses, and even small ones in some individuals, will cause **circulatory changes** in the brain, ears and eyes which are responsible for the symptoms of overdosing connected with these organs. The exact nature and cause of the interference with the circulation in these organs is not well understood. Large doses, or even the long continued use of moderate ones may cause degenerative changes in the optic and auditory nerves and thereby cause blindness or deafness.

Common therapeutic uses of this group of drugs are: **Locally,** Thiersch solution and a number of non-official combinations of salicylic acid are used as antiseptic washes.

Alcoholic solutions of salicylic acid are used as washes to check excessive localized perspiration, as of the hands or feet, and salicylic acid powder, diluted with equal parts of boracic acid is placed in the shoes to inhibit perspiration of the feet.

In collodion, plasters and pastes, salicylic acid is used to soften corns.

Salicylic ointment is used in skin diseases.

The volatile oils of wintergreen and birch, methyl and ethyl salicylate, mesotan and spirosal are applied to the skin both for their counterirritant effects and for their salicylic action after absorption.

Internal Uses.—To relieve the conditions present in acute articular rheumatism, tonsillitis, pleurisy, and similar affections.

To lessen pain in gout and chronic affections of the joints, lumbago, neuritis, etc.

To reduce congestions that are conducive to colds.

Toxicology:

Symptoms of poisoning (which may be induced by one excessive dose or the continued use of moderate doses) are: nausea, vomiting and sometimes diarrhea; ringing in the ears and, in extreme cases, deafness. More rarely, there may be disturbance of vision followed, in severe cases, by blindness. Headache, extreme restlessness and delirium or mental dullness and apathy. There may be a rash. Albumin and casts will be found in the urine. The more pronounced symptoms are particularly likely to occur following the use of a poisonous dose and, in such case, conditions of collapse are more or less marked, but death from poisoning by these drugs is rare.

The special points in the treatment for poisoning are: To take the usual means to prevent collapse and, if necessary, give sedatives, as bromides, to check nervous excitement.

Salol is decomposed in the intestine into salicylic acid and carbolic acid and thus in poisoning there will be symptoms of carbolic acid poisoning, as well as those of salicylic acid, and the treatment must include that for carbolic acid poisoning.

Aspirin, which is usually less likely to have untoward effects than the alkaline salicylates, will at times, due to idiosyncrasy, produce the following effects, even in moderate doses: Edema of the face and neck and, sometimes, the upper part of the chest and the mucous membrane of the nose and throat; urticaria, nausea and vomiting; dizziness; more or less pronounced collapse. The causes of these symptoms are unknown.

ANTIARTHRITICS

Antiarthritics are remedies used to cure or relieve gout. Those in common use are: Atophan, known also as *cinchophen*, phenylquininoline carbonic acid and *phenylcinchoninic acid*, this is described under diuretics. Salicylic acid, previously described, and colchicum.

Colchicum is obtained from the meadow saffron, a crocus-like plant. Its active principle is *colchicine.*

Preparations made from the corm or bulb are:

Colchicum corm, 4 grs. (0.25 gm.).
Extract, 1 gr. (0.06 gm.).
Wine (40 per cent.), 10–30 m. (0.6–2.0 c.c.).

Preparations of the seed are:

Colchicum seed, 3 grs. (0.2 gm.).
Fluidextract, 3m. (0.2 c.c.).
Tincture, 30 m. (2.0 c.c.).
Wine (10 per cent.), 20 m. –1ʒ (1.0–4.0 c.c.).
Colchicina, $\frac{1}{120}$ gr. (0.0005 gm.).

Action and Effects.—Colchicum is very irritant to mucous membranes and in susceptible individuals, even therapeutic doses will cause nausea and vomiting and diarrhea, and, in poisoning, there will be blood in the vomitus and feces and intense abdominal pain. It irritates the kidneys during elimination and thus causes diuresis. It lessens the pain and inflammation around the joints in gout, but how it does so is not known.

In poisoning, in addition to the local symptoms, there will be a progressive paralysis associated with apathy and symptoms of collapse, and death may occur from paralysis of the respiratory muscles. It is not known if the depression is due to a direct action on the nervous system or if it is the result of the gastro-intestinal conditions on the nervous system.

THE PHENOL COMPOUNDS

CARBOLIC ACID OR PHENOL

Carbolic acid or phenol is obtained from coal tar by fractional distillation, also, it is prepared synthetically. A number of drugs obtained from the tars resemble carbolic acid in their composition and actions and these are classed in chemistry as phenols.

Preparations.—Carbolic acid crystals, 96 per cent.

Liquefied phenol, 90 per cent., *made by heating, and thus melting, the crystals and adding* 10 *parts of water to* 90 *of crystals. This is readily soluble in alcohol, but it will not remain in solution in water unless diluted sufficiently to make at least a* 5 *per cent. solution. If less water than this is used some of the phenol will separate in oil-like globules. Phenol is rarely used internally unless compounded with other drugs, as in salol, but, occasionally, it is given in a* **dose** of 1 m. (0.06 c.c.) *of liquefied phenol or the equivalent in its solutions. The dose must be diluted to make a* ½ *per cent. solution.*

As a disinfectant, phenol is used in 2–5 per cent. solutions, as an antiseptic irrigation it is generally used in ½–1 per cent. solutions.

Ointment, 3 per cent.

Glycerite of phenol, *a* 20 *per cent. solution of carbolic acid in glycerine.*

Dobell's solution *which consists of* 3 *per cent. phenol, sodium bicarbonate and borax a.a.* 1.5 *per cent., water and glycerine. This is used as a mouth wash in* 2–5 *per cent. solutions.*

Fate in the Body.—Phenol is readily absorbed from wounds and mucous membranes and, to a slight degree, through the skin. It is oxidized in the body and the

products of oxidation are eliminated in the urine. When present in large amounts, as in poisoning, they give the urine a smoky greenish, appearance and, if the urine is allowed to stand it will become dark brown or black due to the further oxidation of these compounds.

Actions.—Carbolic precipitates protein and, by so doing, it acts as a general protoplasmic poison. It does not form a hard coagulum with the protein as the metal salts do and, therefore, it has greater penetrating power. It tends to first stimulate and then depress protoplasm. It destroys soft tissues more readily than the skin and, after absorption, it is the nerve-centers, heart muscle and kidneys that are chiefly affected.

Effects of Action—On Bacteria.—Phenol will arrest the activity of bacteria, *i.e.*, it will act as an antiseptic, in dilutions as weak as 1 : 500, and in a strength of 2 per cent., it will destroy non-sporulating organisms in a few minutes, if they are exposed to its influence, and not embedded in blood, pus, excreta, etc., but even a 5 per cent. solution will require from 20–30 minutes to act as a disinfectant under such circumstances and will have practically no effect upon spores.

On the skin, even a 5 per cent. solution, if allowed to evaporate, will have no other effect (aside from its disinfectant action) than to cause redness and sensations of irritation and tingling followed by a tendency to local anesthesia. If, however, a solution even as dilute as 2 per cent. and possibly weaker, is kept in contact with the skin for some time and its evaporation prevented, as when thick compresses are used for a *carbolic dressing* or when the compresses are covered with oil muslin or other fabric that interferes with evaporation, a so-called *burn* may result. Such *burns* are likely to be very deep and difficult to heal and may result in gangrene. As the phenol acts as a local anesthetic, the escharotic action of the solution may proceed without causing pain. Thus, though there are few drugs that will, by their local action, relieve itching and lessen pain due to local inflammation,

as readily as carbolic it is now rarely used for these purposes in aqueous solution. The ointment and glycerite, however, are sometimes used as antiseptic antipruritics (to allay itching) for the fat and glycerine lessen the escharotic tendency of the carbolic. Liquefied phenol or the globules that separate from improperly prepared solutions will destroy skin almost instantly, unless their action is neutralized.

At one time carbolic solutions were much used for the irrigation of wounds but it was found that the phenol action on the tissue cells was deleterious and tended to retard healing.

The action on mucous membranes is similar to that on the skin but the destruction of the membrane is more easily affected. When taken by mouth, a small amount of a dilute solution tends, by its local anesthetic action, to allay nausea, but a slight overdose will, by its irritant action on the membrane, induce nausea and vomiting.

Carbolic is not used intentionally for its **effects after absorption,** but, as it is readily absorbed, these may occur from its external use and in poisoning. They consist of a transitory stimulation of the heart muscle and nerve-centers followed, if more than a very small amount is absorbed, by depression and by irritation of the urinary tract. Thus, the absorption of a very small quantity will cause an increase in the rate and strength of the pulse and in the rate and depth of breathing and a slight reduction of temperature, especially if there is fever, (due, it is thought, to increased sensitiveness of the heat regulating centers) and increased secretion of urine. These effects, if more than a small amount is absorbed, are followed by apathy and slowing and weakening of the pulse and breathing.

Carbolic is used: To disinfect excreta, toilets, sinks and the like, and linen. It does not destroy fabrics nor corrode metal.

A small amount of the liquefied phenol is sometimes swabbed over a small local area when a powerful disinfectant or cautic is needed. After the desired degree of

action has been obtained the part is swabbed with alcohol or oil to remove the carbolic and prevent its penetration.

Dilute solutions are sometimes used as antiseptic douches.

The ointment especially is sometimes used to lessen pruritus (itching).

Occasionally carbolic is given by mouth to lessen nausea.

Toxicology:

The symptoms of poisoning depend upon the concentration of the solution used. If a concentrated solution is swallowed, the membrane of the mouth and throat becomes white and blanched and there are the usual symptoms produced by irritant drugs. As a rule, however, convulsions do not occur, because of the rapid depression of nerve centers and, also because of this, collapse is likely to be pronounced. There will be excessive secretion of saliva, tears and perspiration, but this is thought to be the result of the nausea.

If toxic amounts of a dilute solution are taken, the symptoms will be due to the effects of the drug after absorption and will consist of those mentioned on the preceding page followed by profound collapse. Death is likely to occur in a very short time from paralysis of the heart or of the respiratory center.

Treatment for Poisoning.—If concentrated carbolic is spilled on the skin the part should be at once washed with alcohol or, if this cannot be obtained, a bland oil. When a concentrated solution (above 1 per cent.) is swallowed, whiskey or other beverages containing as much as 20 per cent. alcohol—or even ethyl alcohol diluted to 20 per cent. —is given, but the stomach must be lavaged at once because, though the alcohol will prevent the local corrosive action of the carbolic, it will hasten its absorption and it does not prevent its actions after absorption. Milk, white of egg or other demulcent is given and sometimes a dose of either sodium or magnesium sulphate in a glass of water, because carbolic has a slight tendency to unite with sulphur and the resulting sulphocarbolates are relatively

harmless. Sodium sulphate (not magnesium)[1] is added to normal saline solution if this is given intravenously to help overcome collapse and flush the kidneys. Caffeine, strychnine and atropine are sometimes prescribed to prevent collapse. If a toxic amount of a very dilute solution is used, the alcohol is omitted, otherwise the treatment is the same as for poisoning by concentrated solutions. If the poisoning is due to the absorption of carbolic from wounds, the dressing is removed and the wound irrigated and the usual means taken to prevent collapse and irritation of the kidneys.

CRESOLS

The cresols of which there are three isomeric[2] forms are procured chiefly from coal tar. All three are generally contained in the various preparations of cresols as they can only be separated by an expensive method.

Cresol or **tricresol, dose** for internal use, 1 m. (0.06 c.c.). As a disinfectant cresol is generally used in from 1–3 per cent. solutions.

Cresol is a simple preparation of the cresols, it resembles phenol in its composition and actions but is said to be less poisonous, though it is from three to four times as active a germicide. Its value as a disinfectant, however, in its natural form is restricted because it does not mix readily with water, but, as it is soluble in soap solutions, various combinations of soap and cresol are used and they serve both as disinfectants and detergents. Cresol is occasionally used internally, as a gastro-intestinal antiseptic, to lessen fermentation and putrefaction.

The most commonly used compounds of cresol and soap are: Compound solution of cresol which is used in 5 per cent. solutions as a disinfectant, chiefly for the skin, utensils and the like, and in ½–1 per cent. solutions for antiseptic vaginal douches.

[1] Why not magnesium sulphate? If unable to answer see description of magnesium sulphate under Anesthetics.

[2] Isomers, it will be remembered, are substances consisting of the same elements, in the same proportion, but differently arranged in the molecule so that the nature of the isomers is not identical.

Lysol, which is used in the same per cents. and for the same purposes as the compound cresol solution.

Creoline, which acts as a deodorant, as well as a disinfectant, and is therefore used especially to disinfect excreta, toilets, bed-pans and similar utensils. It is also used in ½–1 per cent. solutions for vaginal douches. Warm (*not hot*) water must be used for preparing solutions of creoline.

PICRIC ACID OR TRINITROPHENOL

Picric acid is prepared by nitrating phenol. It resembles carbolic acid in its **action,** but it is less caustic, though more anesthetic, and it is astringent. It is now very commonly **used,** in about a 5 per cent. alcoholic solution, on the skin in preparation for operation, as a substitute for iodine, and, in weaker solutions, usually about 1 per cent., it is used as an antiseptic, on mucous membranes, for vaginal douches, the cleansing of wounds, and as a dressing for burns. Its special value for such a dressing is that, after a very transitory smarting, it acts as an anodyne. A common method of using it for the purpose is to saturate gauze compresses with the solution and, after applying them to the burned area, cover them with cotton and bandage the dressing in place. Picric acid can not be used in this way for large areas, because enough of the acid may be absorbed to cause poisoning. **The symptoms of poisoning** are similar to those of carbolic acid and, in addition, the skin and mucous membranes assume a yellow tint, resembling jaundice and the urine is likely to have a red tinge. Even quite small amounts taken by mouth, may cause nausea, vomiting and diarrhea.

RESORCIN

Dose, 2 grs. (0.13 gm.).

Resorcin is prepared from carbolic acid and resembles the latter in its **actions** but it is less caustic. After absorption, however, in addition to the systemic effects produced by carbolic, resorcin is likely to act upon the hemoglobin of the red corpuscles, forming methemoglobin,

and thus interfere with the oxygen carrying power of the blood which, if large doses are taken, greatly increases the danger of collapse. Resorcin is used chiefly as an external application, in solutions of from 1–10 per cent., to relieve itching and as an antiparasitic in some skin diseases, especially conditions of the scalp which cause dandruff and baldness. It is sometimes added to the paraffines used in the treatment of burns and, occasionally, it is given by mouth to check the activity of bacteria in the alimentary canal and thus lessen fermentation and putrefaction.

NAPHTHOLS AND NAPHTHALIN

The naphthols are derived from naphthalin, a coal tar product. They resemble carbolic in their composition and actions, but are less caustic though exceedingly irritating, and more strongly antiseptic. There are two distinct naphthols, known as *alpha-naphthol* and *beta-naphthol*. The former, though a more active germicide than the latter, is more poisonous, and it is the beta-naphthol that is generally used in therapeutics. It is employed chiefly as a local application, usually in ointment, in the treatment of parasitic skin diseases and as an addition to the paraffines used for the treatment of burns. It is occasionally given by mouth to act as an intestinal antiseptic, either alone or with other drugs for similar action as benzoic and salicylic acid.

Dose, 3–10 grs. (0.2–0.6 gm.).

PYROGALLOL OR PYROGALLIC ACID

This is prepared from gallic acid. Its chemical composition and its actions are similar to those of carbolic acid. It is used chiefly in the treatment of parasitic skin diseases, usually in ointment in strengths of 5–10 per cent.

CREOSOTE (CREOSOTUM) AND GUAIACOL

Creosote is a rather volatile substance obtained by the distillation of wood-tar. It is a mixture of phenol and phenol derivatives, chiefly cresols and guaiacol.

Preparations and dosage:
Creosote, 2, 5 m. (0.13–0.3 c.c.).
Creosote carbonate, 15 grs. (1.0 gm.).
Guaiacol, 8 m. (0.5 c.c.).
Guaiacol carbonate (*duotol*), 15 grs. (1.0 gm.).

For local action in the respiratory organs, creosote is commonly **given** by inhalation, either being added to boiling water and the steam inhaled or dropped on the sponge in a mask inhaler and the latter placed over the mouth. **For internal use,** these drugs are generally given in capsules or else combined with other drugs. Their **actions** are very similar to those of carbolic acid, but they are less corrosive. They are **used** chiefly as intestinal antiseptics, but they are excreted through the kidneys and may also act as urinary antiseptics. Creosote is also excreted through the respiratory tract and, because of this, it was formerly much used in the treatment of tuberculosis, but, as the tubercle bacilli are embedded in the lung substance it is thought that creosote cannot reach them. It acts, however, as an expectorant and it is thought that the benefit derived from its use in tuberculosis is due to this action and also its antipyretic effect and the reduction of fermentation and putrefaction in the stomach and intestines. Guaiacol is occasionally used, diluted with glycerine, as a counterirritant in the treatment of rheumatism.

BALSAMS OF BENZOIN, PERU AND TOLU

BENZOIC AND CINNAMIC ACIDS AND THEIR SALTS

Balsams are mixtures of resins (gum-like substances) benzoic and cinnamic acids and salts of these acids (benzoates and cinnamates) and various aromatic substances of the volatile oil type. The true balsams[1] commonly used in therapeutics are balsam of benzoin, balsam of Peru and balsam of Tolu. They are obtained from different species of fir trees.

Preparations of balsam of benzoin are:

Tincture of benzoin, ½–1 ʒ (2.0–4.0 c.c.).

Compound tincture of benzoin, 1–2 ʒ (4.0–8.0 c.c.). This contains the *alcohol soluble constituents of balsam of benzoin, aloes, storax and balsam of Tolu.*

Benzoic acid, 5–15 grs. (0.3–1.0 gm.).

Ammonium benzoate, 5–15 grs. (0.3–1.0 gm.).

Sodium benzoate, 5–15 grs. (0.3–1.0 gm.).

Cinnamic acid and its salts are rarely used.

Actions and Effects.—Benzoic and cinnamic acids are slightly irritant to the skin and more so to mucous membranes and raw surface, but the consequent smarting is followed by a slight analgesia, because of the depression of sensory nerve-endings. The actions of these acids and of their salts after absorption are similar to those of salicylic acid and the salicylates.

Benzoic acid and the benzoates are **used** chiefly as intestinal and urinary antiseptics and, occasionally, as substitutes for salicylic acid and the salicylates in the treatment of rheumatism. They have also been widely used as food preservatives, but their use is now prohibited

[1] Some of the oleoresins, especially copaiba, are often referred to, though erroneously, as balsams.

because, in small amounts they retard the activity of the digestive ferments and thus of digestion and in overdoses they are poisonous. The symptoms of poisoning are similar to those produced by salicylic acid.

Benzoin owes its effects chiefly to benzoic and cinnamic acids and their salts, and, therefore, it is somewhat irritant (though less so than the acids) and, subsequently, analgesic. Like most other volatile drugs it is excreted to some extent through the lungs. It is used chiefly as an expectorant and a stimulant, though soothing, antiseptic, application for mucous membranes, ulcers, pressure-sores and the like. For its action on the respiratory organs it is very commonly added to boiling water and the steam inhaled.

As balsam of Peru has the same active principles as benzoin its actions are similar, but it is not as volatile and is not excreted through the lungs to the same extent. It is used chiefly for local applications to ulcers and similar sores as an antiseptic, soothing tissue stimulant.[1]

Balsam of Tolu only contains very small amounts of the active principles. It is used chiefly as an ingredient of expectorant and cough mixtures, but it is thought that its agreeable flavor is its chief asset.

[1] The reason why slightly irritant substances, that do not induce irritation in a manner injurious to tissue cells, will act as tissue stimulants, was given on page 49.

TAR (PIX LIQUIDA)

Dosage:
Oil of tar, 1–5 m. (0.06–0.3 c.c.).
Syrup of tar, 1℥ (4 c.c.).

Tar is a black, thick, semi-liquid oleoresin obtained by the destructive distillation of the wood of certain species of pine trees. A number of substances can be separated from it by further distillation, such as the volatile oil of tar, creosote, and similar compounds. Tar acts as an irritant, antiseptic and a parasiticide. Its volatile substances are partly excreted through the respiratory organs and the volatile oil and a 7 per cent. syrup of the tar are **used** as expectorants. Tar ointment is employed in the treatment of various skin diseases of parasitic origin. The condition of it must be watched when tar is used, because, though it is not as caustic as carbolic, it is sufficiently irritant, even to the skin, to cause inflammation.

CHRYSAROBIN

Chrysarobin is obtained from Goa powder, a substance found in the wood of the *Andira araroba*, a tropical tree. **The local actions** are similar to those of tar and it is **used** externally for the same purpose; *i.e.*, in the treatment of skin diseases, especially those of parasitic origin. It is used chiefly in ointment and in 2–10 per cent. solutions. It is even more irritant than tar and it stains the skin, nails, and clothing brown, and the hair a greenish yellow. The stain can be removed by washing it with a dilute solution of caustic soda or of chlorinated soda.

CHLORINE COMPOUNDS

Chlorine is a gaseous element. It does not occur free in nature, but it is widely distributed in the form of salts, especially the chlorides, of sodium, potassium, calcium and magnesium.

Chlorine combines very readily with hydrogen and thus forms hydrochloric acid. It also unites with oxygen and hydrogen to form four different acids. The names of the acids and their salts made by these different combinations are:

Composition	Acids	Salts
HCl	Hydrochloric	Chlorides
HClO	Hypochlorous	Hypochlorites
$HClO_2$	Chlorous	Chlorites
$HClO_3$	Chloric	Chlorates
$HClO_4$	Perchloric	Perchlorates

Hydrochloric acid and some of its salts (*e.g.*, sodium chloride) do not part with their chlorine under ordinary circumstances and thus their actions are due solely to their acid or salt action, but the other acids and many of their salts and other preparations are unstable and part readily with their chlorine. Some of those which do are very widely used, both in industries and therapeutics, as a convenient way of utilizing chlorine, which is too dangerous in its gaseous form for common use.

Actions of Chlorine.—Chlorine unites with protein and thereby destroys tissue and bacteria. It does not form a hard coagulum, like the metal salts, but tends rather to dissolve the protein; the result, however, is intensely irritating and readily fatal. Air containing as small an amount as 1 part in 100,000 is exceedingly irritating to the eyes

and respiratory passages and slightly higher concentrations will cause intense congestion of the respiratory passages and lungs with consequent hemorrhages, pain, dyspane and even death, by inducing an asphyxiating degree of inflammation and edema of the respiratory organs. Also, chlorine is a powerful oxidizing agent, it acts as such because it has an intense affinity for hydrogen and will take it from steam and boiling water,[1] thus setting free the oxygen of the water which then combines with organic matter present and decomposes it. Because of its oxidizing properties chlorine destroys colors and acts as a deodorant.

The chlorine compounds used in therapeutics for the effects of their chlorine are: Chlorinated lime, hypochlorous acid and hypochlorites, chloramine-T., dichloramine-T., eupad, eusol and halazone.

Chlorinated lime, commonly known as *chloride of lime,* sets free chlorine as soon as it is moistened. It is very irritant and it destroys most fabrics. In its natural form it is used chiefly as a disinfectant for excreta, toilets and the like.

Of the hypochlorites, potassium hypochlorite or *eau de Javelle* and the commercial solution of **sodium hypochlorite,** commonly known as *Labarraque's solution* are too irritant for use about the body and are expensive to use for the disinfection of excreta, etc., and thus they are not much used in therapeutics, but the former, especially, is very widely employed as a bleaching agent in laundries and certain manufacturing processes. **Neutral sodium hypochlorite,** commonly known as *Dakin's solution,*[2] however, was, during the war, found to be one of the best disinfectants for infected wounds. If properly prepared, it not only destroys bacteria but it also tends to decompose their toxins and necrotic tissue, and, nevertheless, is not as irritant to healthy tissue as Labarraque's solution.

[1] Neither the extraction of hydrogen from water nor the union of oxygen with matter take place readily at low temperatures.

[2] Dr. Dakin was one of the first chemists to find the means of preparing a solution of hypochlorites having the advantages, without the corrosive action of the other hypochlorites.

It is however sufficiently irritating to make it necessary to protect the skin around a wound for which it is used. The means of doing this and the Carrel method of using Dakin's solution are described in all up-to-date text-books of nursing procedure and, therefore space will not be taken to do so here. Dakin's solution is generally used for wounds in the strength of 0.5 per cent. As the chlorine combines with the protein of the blood and tissues in the wound, and the resulting compounds have no germicidal action, the solution used in a wound is soon rendered inert and, therefore must be constantly renewed as it is when the Carrel technique is accurately carried out.

Chloramine-T is an abbreviated name for *paratoluenesulphondichloramine.* It is less irritating, but more strongly germicidal than Dakin's solution, but it does not dissolve the necrosed tissue commonly present in infected and contused wounds as well as the latter. Chloramine-T may be used in an aqueous solution, or it may be employed dry, impregnated in gauze (which is moistened if necessary), or in the form of a paste in which it is mixed with a soap-like substance known as *sodium stearate.* The strength of the solution used in wounds is, as a rule, 2 per cent. but it may be used in strengths up to 3 per cent. The strength of solutions used for irrigation of the eye is usually 1:1000; that of solutions for irrigation of mucous lined cavities, as the bladder, nose, throat, 1:500, but stronger solutions are sometimes employed in severe infections.

Chlorazene is the name for a proprietary preparation of chloramine-T.

Dichloramine-T is the abbreviated name for *paratoluenesulphondichloramine.* As its name implies (di signifies two) it contains more chlorine than chloramine-T. It is a very active germicide and it dissolves necrotic tissue, stimulates granulation and, as usually prepared, it prevents dressings sticking to the wound and, therefore, injury to the granulations during the removal of the dressings. Dichloramine-T is only sparingly soluble in water and is generally dissolved in **chlorcosane,** which is an oil obtained

by the chlorination of paraffine wax) or in mixtures of eucalyptol and paraffine that have been treated with chlorine. Solutions of dichloramine-T must be kept in amber-colored bottles for they are decomposed by light and the other colored glasses used for bottles do not shut out the rays which cause their decomposition. The strengths of the solutions commonly used are 5–8 per cent. In the treatment of wounds, the solution may be poured into the wound or, especially for superficial wounds and sores, gauze saturated with it may be laid over the part; for such cavities as the nose and throat, the solution is generally sprayed from an atomizer. An atomizer with a hard-rubber tube (and no metal) must be used, as dichloramine-T, like other chlorine disinfectants, corrodes metal.

Halazone, which is *parasulphondichloraminobenzoic acid,* is used for the disinfection of drinking water. It is said to be efficacious in the proportion of 1 part to 4,000,000 of water.

Eupad is a powdered preparation of chloride of lime and boric acid; when moistened it liberates hydrochlorous acid. **Eusol** is a solution of eupad. Hydrochlorous acid is very irritant and thus the same care is necessary in the use of these disinfectants as of Dakin's solution.

Antiformin is a new preparation of sodium hypochlorite that dissolves such organic matter as that of feces, sputum, disintegrated tissues and the bodies of many species of bacteria. It does, however, destroy the bacillus tuberculosis.

OXIDIZING AGENTS

Drugs which act as oxidizing agents do so either because they have oxygen in loose combination and part with it readily or else, as in the case of chlorine, they liberate oxygen from compounds, especially water, with which they come in contact.

The drugs most commonly used in therapeutics for their oxidizing properties are hydrogen peroxide, permanganate of potash (see under Manganese) and chromic acid.

Hydrogen peroxide (H_2O_2) is readily decomposed to water and oxygen especially in the presence of organic substances, such as blood, pus and muscle juice, which contain catalyses that hasten decomposition. The liberated gas unites with the material that it comes in contact with and decomposes it. Its action is most marked on such substances as pus and necrosed tissue and, especially during the decomposition of such substances an active effervescence occurs. Hydrogen peroxide also destroys bacteria, but, in a wound, its germicidal action is quickly lost because of its combination with other material. It causes temporary sensations of stinging and smarting due to the heat evolved in the chemical interaction. Peroxide of hydrogen is used chiefly to loosen dried substances and adhesive plaster and thus facilitate the removal of adherent dressings from wounds; to rid the mouth and throat of sores and suppurative matter and, occasionally, to rid wounds of pus and necrotic tissue.

Chromic acid (*chromium trioxide*) either in solid form or in aqueous solution is used as a caustic.

REDUCING AGENTS

The process of reduction is the opposite of oxidation, *i.e.*, it is the removal of oxygen from matter. The reducing agents used in therapeutics are sulphurous acid and sulphur dioxide. By removing oxygen from matter these substances act as bleaching agents, antiseptics and parasiticides. Sulphurous acid is the more powerful reducer of the two. It is formed when sulphur dioxide is dissolved in water. Sulphur dioxide is formed when the element sulphur is burned in air. It is a colorless gas that is very easily condensed to a liquid. It is very irritating to mucous membranes and the eyes. It and sulphurous acid are particularly destructive to vermin and, for this reason, sulphur is burned in rooms that are infested with bed-bugs. The vessel in which the sulphur is placed for the purpose is generally stood in a pail of boiling water for the steam from the water and the gas from the sulphur (sulphur dioxide) unite to form the more active and penetrating parasiticide, sulphurous acid.

SULPHIDES, THIOL, ICHTHYOL

The element sulphur is very active and, in the intestines or when it is kept in contact with the skin, it unites readily with hydrogen and other elements that it abstracts from matter and forms sulphides. **The sulphides** are somewhat irritant to mucous membranes and raw surfaces and they are antiseptic and particularly destructive to the organism that causes scabies (*itch*). The use of sulphur as a cathartic has been already described. For use on the skin it is generally employed in the form of ointment or lotion.

Thiol is prepared by the action of sulphur on tar. It is used in powder form and in solution as an antiseptic and parasiticide in skin diseases.

Ichthyol is an asphalt-like material of which deposits exist in several parts of the world, but chiefly in the Tyrol, where they have developed by the decomposition of fossil fish. It contains sulphur, this being an ordinary constituent of protein and, therefore, of decomposed nitrogenous substances. Various compounds of ichthyol are used as antiseptics and parasiticides in the treatment of skin diseases.

FORMALDEHYD

Formaldehyd is a gas that is used for its germicidal properties. It is obtained chiefly by the oxidation of wood (methyl) alcohol. At a low temperature the gas is precipitated as a white powder, known as *paraformaldehyd.* This is used in compressed forms as a means of marketing the formaldehyd for use as a gaseous disinfectant, for, on being heated, it is reconverted into gas. Formaldehyd gas is soluble in water in between 37 and 40 per cent. solution. The solution of formaldehyd is very commonly known as *formalin.* Formaldehyd is very irritating to mucous membranes, the eyes and wounds, and strong solutions will dry and harden tissue, even the skin. **Formalin 37–40 per cent. is used chiefly in** laboratories, for the preservation of specimens, and as a stock solution. **Solutions of between 5 and 10 per cents. are sometimes used** as local bathing lotions to check excessive perspiration and they are used to disinfect linen, nonmetals, utensils and excreta. The material being disinfected must be kept covered (to avoid the escape of the gas) and exposed to the influence of the disinfectant for from 20–30 minutes. The irritant action of the gas which passes from a solution is a great objection to the use of formalin and the new phenol and chlorine compounds are now more commonly used for most of the above purposes. **Solutions of formalin as weak as 1: 2000** will inhibit the activity of the lactic acid bacilli which cause souring of milk and formalin has therefore been much used as a milk preservative, but its use for the purpose has been condemned for, even in such weak solution, it lessens the activity of the digestive ferments and thus may retard digestion sufficiently to promote digestive disturbances in infants and young children. **Formaldehyd gas has**

been much used for the disinfection of rooms that have been occupied by persons suffering with readily communicable diseases, but, for the present, bacteriologists believe that such disinfection is unnecessary. As formaldehyd does not injure the majority of colors nor the fabrics of which clothing, blankets and the like are made, it is quite commonly used for their disinfection. For the purpose, the articles must be placed in a tightly sealed room or cupboard and so arranged that all surfaces are exposed to the influence of the gas, for the latter has very little penetrating power, and exposure to the influence of the gas for 12 hours is necessary. The gas may be evolved from wood alcohol, or by burning the solid paraformaldehyd or by heating formalin and the heat may be supplied by adding the formalin to a compound, such as potassium permanganate, which reacts readily with the latter for, as the result of the reaction intense heat is produced. As in the case of sulphur, moisture must be provided and the room kept warm. For further information regarding these methods of disinfection see a textbook of bacteriology. Formaldehyd is rendered inert by alkalies, especially ammonia, and, therefore, exposing ammonia in a room that has been fumigated with formaldehyd, will free it of odor and diluted ammonia is used as a chemical antidote for poisoning by formaldehyd. The symptoms of poisoning and the treatment are the same as for other irritants.

HEXAMETHYLENAMINE OR UROTROPIN

Formaldehyd is an excellent disinfectant for the urinary tract, but formalin is too irritant to the alimentary canal to be used and, therefore, hexamethylenamine, commonly known by the trade name of *urotropin* and, sometimes as *aminoformin* and *formin*, is used. This only liberates formaldehyd when it comes in contact with acid. Thus, if it is given when there is no free acid in the stomach, as when the latter is empty, formaldehyd will not be liberated

until the drug is in the urine. It is given with large quantities of water to further its elimination by the kidneys. If, as is often the case when septic conditions of the urinary organs exist, the urine is alkaline, acid sodium phosphate, which renders the acid, is prescribed, but it must not be administered at the same time as the urotropin. If urotropin is given when there is acid in the stomach some of the formaldehyd will be liberated and, because of its irritant action, it may induce nausea and vomiting. Too large doses of urotropin will induce intense irritation of the urinary organs and there may be blood, casts and albumin in the urine.

Preparations and dosages:

Hexamethylenamine (*urotropin*), 5–20 grs. (0.3–1.3 gm.).

Helmitol or *hexamethylenamine-methylencitras*, 5–15 grs. (0.3–1.0 gm.).

Saliformin or hexamethylenamine salicylas, 5–30 grs. (0.3–2.0 gms.).

Hexalet (*hexamethylenamine salicylsulphonic acid*), 15 grs. (1 gm.).

DYES

Many of the dyes used for coloring fabrics are synthesized from compounds that are similar to phenol and other tar and petroleum products. Of these, three have been considerably used in therapeutics, viz., flavin, methylene blue and scarlet red.

Flavin, known also as *acriflavin,* is a yellow dye. It has been considerably used lately as a disinfectant for septic wounds, usually, in a 1: 1000 solution in an 8 per cent. salt solution.

Methylene blue is used to some extent as an antiseptic for the urinary tract in gonorrhea. But its most common uses are to test the functional capacity of the kidneys and the capacity of the liver to destroy toxins.

Dosage, for the liver test, ⅓ gr. (0.02 gm.) for other purposes 2–8 grs. (0.13–0.5 gm.).

It is given by subcutaneous injection or in capsules.

The liver test is based on the fact that, if the liver is functioning properly it will be able to take out and eliminate the small amount of the dye given for the test. Larger amounts are eliminated in the urine and if the kidneys are functioning properly, the pigment should appear in the urine within an hour after its subcutaneous injection

Scarlet red is used occasionally as an antiseptic tissue stimulant for ulcers and sluggish wounds.

SPECIAL USES OF THE VARIOUS ANTISEPTICS AND DISINFECTANTS

By recalling the effects of the various classes of irritant drugs it will be appreciated that, whether they induce irritation by a simple salt action or by causing some pronounced chemical change in protoplasm, such drugs act as antiseptics and the stronger ones also as disinfectants. For various reasons, however, they are not all suited for use as antiseptics and disinfectants and, those which are, are not all equally efficient for the same purposes. Some of the reasons for these facts are: The various species of bacteria are not all equally affected by the same chemicals; some disinfectants act more readily upon microorganisms than upon human tissue, while others are only germicidal in concentrations that are destructive to human tissue or are otherwise poisonous; certain of the antiseptics, when applied to sluggish wounds and sores stimulate granulation, while others cause changes in protoplasm that retard healing and some lose their antiseptic value when they combine with substances in the wound; many of the drugs that are useful disinfectants for certain parts of the body, *e.g.*, the gastro-intestinal and the urinary tracts, also affect other organs in ways that at times may be undesirable, while certain ones can be so administered that they have little or no action upon other parts of the body and these are, therefore, much more commonly used; certain disinfectants, because of their action on protein, are useless for the disinfection of excreta,[1] others will destroy or stain metal, fabrics,[1] etc.; some disinfectants are too expensive for common use and others, while not

[1] The pupils should be required to give examples of disinfectants that should not be used for the disinfection of excreta, white linen, and colored fabrics.

themselves particularly expensive, are only soluble in liquids, such as alcohol, that are expensive.

The following lists show the principal uses as antiseptics and disinfectants of the drugs commonly used for such purposes:[1]

For Cesspools and Privy-vaults.—Chlorinated lime, milk of lime, unslaked lime, sulphate of iron.

For Hoppers, Toilets, Bed-pans, and Similar Utensils, and Excreta.—Cresol, lysol, creoline, carbolic acid, chlorinated soda, chlorinated lime, and formaldehyd.

For Instruments.—Alcohol, cresol, lysol, carbolic acid, and, as an addition to water in which instruments are boiled, sodium carbonate.

For White Clothing and Bed-linen.—Chlorinated soda, chlorinated lime, carbolic acid and formaldehyd. The fabrics must be very thoroughly rinsed in several fresh supplies of water after the use of chlorine compound.

For Colored Fabrics.—Formaldehyd gas as described on page 377.

For the Hands.—Alcohol, green soap, lysol, iodine, mercury, chlorinated lime and soda (when these are rubbed on the skin and moistened, chlorine gas is liberated), permanganate of potash which is followed by the use of oxalic acid to remove the stains.

For the Skin in Preparations for Punctures and Incisions.—Alcohol, ether, iodine, picric acid, green soap.

For Use in Wounds.—Dakin's solution and the other chlorine preparations mentioned on pages 369–372; iodine and the iodine compounds prepared for external use, mentioned on page 334, and potassium mercuric iodide; flavine; quinine hydrochloride; hydrogen peroxide; silver compounds; balsam of Peru; sodium chloride may be mentioned here though, in the percentage in which it is generally used for irrigating wounds, it can hardly be called an antiseptic, but it is easily sterilized and, being isotonic with the blood and tissue fluids, it is non-irritant to tissues.

[1] This book being solely concerned with the use of drugs, heat and other physical means of disinfection are not considered.

For Abrasions, Ulcers and Similar Sores Including those Occurring in Parasitic Skin Diseases.—Those used for wounds and picric acid, salicylic acid, tar, sulphur, ichthyol, thiol, resorcin, chrysarobin, pyrogallol, bismuth compounds.

For the Mouth, Etc.—Boric acid, sodium borate, boroglycerine, glycothymoline, listerine, Dobell's solution, eucalyptol, the volatile oils mentioned on page 278, thymol, menthol, camphor, creosote, benzoin, potassium chlorate, sodium bicarbonate, hydrogen peroxide, potassium permanganate.

In Vaginal Douches.—Lysol and other cresol preparations, green soap, carbolic acid, borosal, boric acid, Dakin's solution and other chlorine compounds, iodine, potassium mercuric iodide, silver preparations.

For the Urinary Organs.—Urotropin, and other hexamethylenamine preparations, benzoic acid and its salts, salicylic acid and its salts, cubebs, copaiba, sandalwood oil, methylene blue. For local irrigations, as of the bladder and urethra, the same antiseptics are used as for vaginal douche.

For Intestinal Antiseptics.—Salol, calomel, the drastic cathartics, betanaphthol and compounds of this drug, ipecac and emetine are used in amœbic dysentery. For local cleansing of the rectum, the antiseptics used as vaginal douches.

For Drinking Water.—Chlorine gas, sodium hypochlorite and, for small quantities, halazone. Copper sulphate is used for the destruction of certain algea, which sometimes infest reservoirs and other water-supply sources.

For Food.—Salt, concentrated sugar, spices are the legitimate preservatives, but boric acid, borax, salicylic acid, formaldehyd and benzoic acid and benzoates are commonly, though, illegally, used.

DIURETICS

Diuretics are agents used to increase the secretion of urine. The various **ways in which they do so** were mentioned on page 58. As there stated, diuresis is induced by a number of drugs that are used for other therapeutic purposes; in fact there are very few drugs employed exclusively as diuretics.

The purposes for which diuretics are most commonly used intentionally are: (1) To stimulate the kidneys when, for any reason, they are inactive; (2) to remove water from the blood and thus, by raising its concentration, increase the absorption of fluid from the tissues and, thereby, reduce dropsy; (3) to further the removal of poisons from the body, either those ingested or those formed within the body; (4) to dilute the urine in order either to lessen the irritant action of poisons on the urinary organs or of the urine on the bladder or other urinary passages when they are inflamed.

Preparations and dosage of drugs which stimulate without irritating, the kidneys:

Caffeine, see page 85.

Theobromine, 5–8 grs. (0.3–0.5 gm.).

Theobromine sodium salicylate or *diuretin.*
Theobromine sodium acetate or *agurin.*
Theobromine lithium benzoate or *urophen b.*
Theobromine lithium salicylate or *urophen s.*

The usual dosage of these double salts of theobromine is 8–15 grs. (0.5–1.0 gm.) but diuretin is occasionally used in much larger doses up to 120 grs. (8.0 gm.).

Theobromine sodium formate or *theophorin,* 8 grs. (0.5 gm.).

Theophyllin sodium acetate, 3–5 grs. (0.2–0.3 gm.).

The origin and actions of **caffeine** have already been discussed.

Theobromine is an alkaloid of similar chemical composition to caffeine. It is derived from the cacao bean and is thus a constituent of chocolate and cocoa. Its actions are similar to those of caffeine, but it does not affect the central nervous system as strongly and its diuretic action is more marked. The salts, especially sodium salicylate are now more commonly used than the theobromine because, as the latter is not very soluble, its absorption is uncertain and it is apt to cause gastric disturbances.

Theophyllin is a similar alkaloid to caffeine and theobromine. It is obtained from tea leaves and it is made synthetically. The synthetic preparation is known as *theocin*. The actions of theophyllin are similar to those of theobromine but it is a more powerful diuretic. It is likely to cause gastric irritation and, it is thought, in large doses renal irritation.

The drugs which act as diuretics by irritating the kidney cells are: Calomel, the urinary antiseptics mentioned on page 382, and phenylcinchoninic acid, also a number of other drugs are sometimes classified under this heading, but, they are so rarely used at present, they need not be considered.

Calomel will produce marked diuresis, especially when dropsy exists. Why it does so is not understood, because it is not very readily absorbed from the intestines and, in the doses that are generally used for the purpose, it can hardly promote sufficient irritation to account for the copious diuresis. Opium is sometimes used with calomel when it is employed as a diuretic in order to lessen peristalsis and thus allow a larger amount of the calomel to be absorbed. For dosage see under Mercury.

Phenylcinchoninic acid or *atophan* in addition to inducing marked diuresis increases the elimination of uric acid and, by unknown actions, it lessens the pain of gout. It is therefore very commonly used in this disease both

for its diuretic and analgesic properties. Dose 8 grs. (0.5 gm.). It is given with large quantities of water.

It sometimes cause severe irritation of the alimentary tract with nausea and diarrhea and symptoms of collapse and it may induce a skin eruption.

The drugs commonly used to promote diuresis by improving the circulation are those of the digitalis group and, when the blood-vessels are abnormally contracted, the nitrate salts may act partly in this way. These drugs are all discussed elsewhere.

The drugs commonly used to induce diuresis by increasing the amount of fluid in the blood-vessels are those salts of the alkalies which are most readily absorbed (*i.e.*, sodium and potassium bicarbonate, and the acetates and citrates of sodium, lithium and potassium, especially potassium acetate) and urea. The manner in which these drugs increase the amount of fluid in the vessels is described under Salt Action on page 47.

The dosage of the salts is given in the section on Antacids.

The dose of urea is 10–60 grs. (0.5–4.0 gm.). It may be given in solution or in capsules. Urea is prepared synthetically. It is of similar composition to the urea of urine. It is generally given in capsules.

When diminished excretion of urine is due to some functional disturbance that is not associated with any organic lesion, as is often the case in fever and post-operative anuria, **water** is the only diuretic required and it is a very important diuretic since, by diluting waste and toxic material, it lessens irritation of the kidneys by these substances. It acts as a diuretic because, merely by its presence in the blood, it increases the volume of the latter and hence raises the pressure in the renal vessels.

VACCINES AND SERUMS

From early times it has been realized that, in the case of many of the diseases now known to be caused by bacteria, one attack of a disease confers immunity for that malady, but the reason for this immunity (*i.e.*, resistance to disease) has only been apprehended in recent years and, even yet, is not fully understood. It is believed, however, that, when bacteria gain entrance to the body, a fight ensues between the bacteria and the body. The bacterial weapons consist of the chemical by-products of their metabolism, which vary in nature with different species of bacteria. Those which produce disease are known as *toxins*. The body has several defences some of which are natural constituents of the blood, but others are only called into being as the result of bacterial invasion, and even the former are normally increased by some infections.

The body's most important protectives are: (1) The white cells of the blood known as *phagocytes;* (2) anti-bacterial substances (*i.e.*, substances which act directly upon the bacteria, such as opsonins, bacteriolysins and agglutinins) and (3) antitoxins (*i.e.*, substances which neutralize the toxins produced by bacteria).

What is known as the Ehrlich antitoxin theory, though its accuracy has not been actually proven, is the generally accepted idea regarding the formation of antitoxins. The basic facts of this theory are as follows: Cell protoplasm contains chemical substances, termed *side-chains* or *receptors,* that are essential for the assimilation of food material by the cells. Toxins of certain bacteria also unite with these receptors, but they destroy them. This however, stimulates the cells to form new receptors. If the quantity of toxin is so great that it combines with the receptors as fast as they are made, death will result, but,

if the receptors can be formed more rapidly than the toxins are produced, the latter will be neutralized and recovery is probable. In such case, the cells will not only form the receptors needed at the time, but will produce a superabundance and the spare ones, which are known as *antitoxins*, are given off to the blood. The latter thereby acquires protective properties and, if germs of similar species to those which stimulated the formation of the antitoxins again invade the body, the antitoxins will unite with their toxins and the conditions of disease will not develop. The antitoxins produced by different kinds of bacteria vary and those formed in response to an attack by one species of bacteria will not act upon the toxins of other varieties.

Even less is known of the **nature and generation of the antibacterial substances** than of antitoxins, but, it has been found, in the case of some diseases, the blood of an infected person and, in some cases, of a person who has recovered from a disease, will act in some manner to destroy the bacteria causing the disease. For example, the serum of the blood taken from a person with typhoid will, if added to a culture of the bacilli which cause typhoid, cause the latter to become agglutinated, *i.e.*, they become precipitated in clumps.

When a person's own cells form the protective substances, the immunity gained is termed **active immunity. Active immunity** may be induced by the use of a vaccine, as well as by an attack of a disease. The immunity gained by a vaccine is not as enduring as that brought about by disease, but it lasts, in most cases, from about 2 to 4 years.

A vaccine may consist of toxins, or of dead bacteria, or of living organisms the virulence of which has been attenuated in some way as by drying or by growth in the body of an animal that does not afford as favorable ground for their development as the human being.

Vaccines are sometimes prepared from bacteria or virus taken from the person for whom the vaccine is intended.

These are known as *autogenous vaccines*, those obtained from other sources are usually designated *stock vaccines*.

Passive immunity is that gained by the receipt of antitoxins or antibacterial substances that have been formed in the body of an animal as the result of the latter's vaccination with bacteria or their toxins. In such case, the individual's own body takes no part in the production of the antibodies. Passive immunity is acquired as soon as the protective substances are injected, but is transitory, enduring only a few days, for the injected material is excreted or disintegrated in the manner of other drugs and the individual's own cells have not gained the power of reacting to the bacteria or toxin for protection from which the injection was made.

The remedies used for conferring passive immunity are called, according to their nature, *antitoxin* or *antibacterial serum*, because their active principles are contained in blood serum obtained from the animal whose body produced them. As a rule, the horse is used for the propagation of these protective substances.

Space will not permit of going into the detail of the **procedure followed in obtaining these immunizing serums** but the usual principle is as follows: A horse is injected with a small amount of a toxin or a small number of attenuated bacteria, as the case requires, whereupon, the animal develops a mild attack of the disease which the toxin or bacteria used produce and the specific antibodies are formed in its body as previously described. Upon recovery, the animal is given a larger dose, and so on, until even very large doses bring no response, because its blood contains a large amount of the specific antibodies. Then blood is drawn from, for convenience, the jugular vein. This is clotted and the expressed serum is filtered off and the amount generally used for a dose put up in sterile ampules or syringes.

Antitoxins, vaccines, etc., are used for prophylactic and curative measures and, certain ones to aid in diagnosis. **By a prophylactic measure is meant,** to prevent disease.

Diphtheria antitoxin is given, as a prophylactic measure, to a person who has been exposed to diphtheria; smallpox vaccination is performed without even waiting for exposure to infection; doses of tetanus antitoxin are used if a person has been wounded in a manner likely to cause tetanus; and antirabic (hydrophobia) vaccine is given when an individual is bitten by an animal that is suspected of rabies. Inoculation with these antiserums and vaccines, as a rule, produces little or no disturbance and they have been proven to be very effective prophylactics against particularly fatal and horrible diseases.

Modes of Administration.—Even the soluble antibodies of these serums and vaccines are not readily absorbed from the alimentary tract and some of them are likely to undergo chemical changes if administered by mouth, thus they are given either subcutaneously, intramuscularly, intravenously, or, sometimes (smallpox vaccine and certain ones used for diagnosis) by puncture or scarification of the skin; and, those used to combat toxins or bacteria that affect the central nervous system, may be given intraspinally, following lumbar puncture.

Anaphylaxis.—Following the receipt of vaccines there is normally, if the vaccination is successful, a slight degree of malaise, but, ordinarily, inoculation with an antitoxin or antibacterial serum is not followed by any marked discomfort. Some people, however, are very easily affected by some proteins and, in such individuals, the proteins of the foreign serum may induce what is known as *serum sickness* or *anaphylaxis*, or, in severe cases, *anaphylactic shock*. It has been found that prophylaxis is particularly likely to occur in those who show sensitiveness to other proteins, for example, people who have attacks of erythema or asthma following the use of protein foods to which they have become sensitized and those who have hay-fever if they inhale the pollen of certain plants. When there is any reason to fear hypersensitiveness to proteins, a dose of serum is generally given in divided doses, for example, if the amount of antitoxin, etc.

to be used is contained in 10 c.c. of serum, 0.1 c.c. is administered as the initial dose and double this amount is given hourly until the full quantity has been administered. The patient must be carefully watched and any symptoms of disturbance reported at once.

Common symptoms of mild anaphylaxis are: Slight fever, itching and redness of the skin and urticaria. **Symptoms which indicate a more serious state are:** dyspnea, cyanosis, violent coughing, a sense of constriction about the chest, marked variations in the pulse, fever and skin eruptions.

Summary of the nature, uses and doses of remedies used for conferring immunity:

For passive immunity:

1. **Antitoxin serum,** which consists of serum separated from the blood of a horse that has been immunized against the toxins of bacteria which produce the specified disease. The antitoxin serums in common use are diphtheria antitoxin and tetanus antitoxin. **Modifications of antitoxin serums are:** (*a*) Concentrated antitoxin, in which the protein of the serum with which the antitoxin is combined is removed; (*b*) dried antitoxin, in which the liquid of the serum has been evaporated.

The dosage of the antitoxins is expressed in units; a unit being the amount of antitoxin required to neutralize 100 times the quantity of standard toxin that is required to kill a guinea-pig weighing 250 pounds.

The usual prophylactic dose of diphtheria antitoxins is 1.000 units; the curative dose, 5.000—40.000 units, the larger doses being given when the disease has made considerable progress.

The usual prophylactic dose of tetanus antitoxin is 1500 units, it is given subcutaneously as soon as possible after the wound is received. The curative dose is 3.000–5.000 units, diluted with an equal amount of salt solution and given intraspinally, or about 10.000 units may be given intravenously.

2. **Antibacterial serum,** which consists of serum ob-

tained from the coagulated blood of a horse that had been immunized against a specified strain of bacteria. It contains some substance which will destroy the kind of bacteria that gave rise to its formation. The names of these serums indicate their nature and uses and thus space will not be taken to give them here, nor the dosage, for this and the value of most of these serums is still somewhat undecided.

For active immunity:

1. **Bacterial vaccines,** consisting of suspensions of dead bacteria in physiological salt solution with, usually, a small amount of a preservative. Certain of the bacterial vaccines are known as *sensitized vaccines.* **Sensitized vaccines** are prepared in the same manner as others, except that the bacterial suspensions are treated with the serum of an animal that has been immunized against the species of bacteria in the vaccine. The serum is then removed by centrifugation and the bacterial bodies again suspended in salt solution. This treatment is supposed to make the bacteria more sensitive to the action of the protective forces of the body and thus facilitate their destruction. The strength of these vaccines is generally specified by the number of bacteria contained in the preparation. About the most important bacterial vaccines in common use are the typhoid, pneumococcus, gonococcus, streptococcus, staphylococcus, bacillus coli vaccines. The names indicate their nature and uses. The amount of a vaccine generally used for a dose is put up in sealed ampules or syringes and thus it is not necessary for nurses to learn the dosage.

2. **Smallpox virus vaccine** is prepared from material taken from the pustules of calves who have cowpox or vaccinia. The virus is supposed to contain the living causative organisms of smallpox the virulence of which has been attenuated by growth in the calf, as explained on page 387.

3. **Antirabic vaccine** or virus consists of the virus of rabies (hydrophobia) which has been rendered practi-

cally harmless to man by passage through rabbits. The preparation consists of dried sections of spinal cords taken from inoculated rabbits, preserved in glycerine until required, and then emulsified in physiological salt solution.

4. **Diphtheria toxin-antitoxin,** commonly termed *T.A.*, consists of toxin produced by the bacteria which cause diphtheria put up with enough antitoxin to neutralize the toxin. The antitoxin, however, does not prevent the toxin stimulating the recipient's cells to form antitoxins. Thus it produces active immunity. It usually requires about three weeks to do so, but, when immunity is established, it is believed to endure for 18 months or, possibly, longer.

Schick's diphtheria immunity test is used to determine if a person has sufficient diphtheria antitoxin in their blood to render them immune to diphtheria. It consists in injecting a small amount of diphtheria toxin intradermally. If the person has no free antitoxin in the blood a small circumscribed area of redness and infiltration will appear at the site of injection within 24 to 48 hours. It persists for from 6 to 12 days, is followed by scaling and leaves a brown pigmented spot.

5. **Tuberculins.**—There are a number of these preparations. They are classed as *old tuberculins* and *new tuberculins*. The so-called old tuberculins resemble the original preparation made by Koch and consist of toxins produced by tubercle bacilli. Most of the new tuberculins are prepared from the dried bacilli. New tuberculins, especially, are occasionally used in the treatment of tuberculosis, but both varieties are employed chiefly as an aid to diagnosis. For this purpose, they are now usually given either by hypodermic injection (Koch method), or scarification (Pirquet method), or inunction (Moro test). The reaction that may occur following the Koch method is a slight fever; that to be watched for after the other tests is the appearance of small nodules or papules at the point of application, within from 24–48

hours. A reaction merely indicates that the patient has had tuberculosis at some time, and not, necessarily, that he is suffering from an active process.

6. **Luetin** consists of an extract of killed cultures of several strains of the spirochæta pallida, the causative agent of syphilis. It is used for the diagnosis of syphilis. In a normal person an injection will produce no response or merely a very slight erythematous area about the point of injection, but, if the recipient has syphilis, especially in the third stage of the disease, papules, which may develop into pustules, are likely to appear.

Cultures of various strains of bacilli classed as lacto-bacilli, because they promote the disintegration of lactose (sugar of milk) to lactic acid, are given by mouth either in solid (tablet) or liquid form or in milk in which they have been grown. Their use is based on the supposition that they and their products interfere with the activity of putrefactive bacteria always present in the intestine. Thus they, especially the strain known as the bacilli bulgaricus, have been much used to overcome excessive intestinal putrefaction, but it is now thought to be doubtful if they do so, to any extent, under conditions prevailing in the intestine. However, the fermented milks are more easily digested than plain milk and afford a nutritious food. Slight differences in the preparation of the milk in the strain of bacilli used produce preparations with slightly different qualities that are known by different names, such as Bulgarian milk, matzoon, zoölak, etc.

Solutions of lacto-bacilli are also used for the irrigation of sinuses and cavities, especially the nasal cavity, in the treatment of infection by putrefactive bacteria.

Leucocyte Extract.—This is prepared from exudates produced in the pleural cavities of rabbits and other animals by the injection of an irritant.

Dose, not less than 10 c.c. It is usually furnished in syringes containing this amount and is given subcutaneously.

Leucocyte extract has been found to increase the immunizing power of the recipient and to aid the action of

antitoxins and vaccines. It will be remembered that the leucocytes of the blood and lymph help to protect the body from invasion by bacteria.

Normal horse serum, *i.e.*, serum obtained from the clotted blood of normal horses is sometimes given intravenously, in hemorrhage, to hasten clotting of the blood.

Pollen extracts are aqueous solutions of proteins obtained from the pollen of different plants which are known to cause hay-fever. There are a number of such extracts made, because, as a rule, the protein obtained from one pollen will not overcome sensitiveness due to another; for example, if an individual's hay-fever is due to the ragweed pollen, it will not be overcome by an extract prepared from goldenrod. However, persons subject to hay-fever are very likely to be sensitive to most of those which occur at certain seasons, as spring or fall.

These extracts must be used with care and the dose regulated according to the individual's sensitiveness, for an overdose will cause alarming symptoms, similar to those described under anaphylaxis, and possibly death. To discover which extract to use, the physician generally rubs a small amount of extract into a scratch on the skin, if the individual is sensitive to that pollen an urticaria-like elevation will result. Small amounts—about 5 to 10 drops—of a dilution slightly weaker than will produce a skin reaction are generally used for the initial doses and, first the size of the dose, and then the strength of the solution is gradually increased.

ORGANOTHERAPY
EXTRACTS OF ANIMAL ENDOCRINE GLANDS

By organotherapy is meant the use of extracts of animal organs for therapeutic purposes. The extracts are prepared from the digestive glands and the endocrine (ductless) glands. It is the preparations from the latter source that are discussed in this section, those obtained from the digestive glands being described under Digestants.

As yet very little is known of the way in which the secretions of the various glands produce their effects and, therefore, it is of course impossible to account for the results following the use of the extracts.

THYROID EXTRACT

Thyroid extract is a powder prepared from the thyroid gland of animals, usually sheep. The thyroid, it will be remembered, is a two-lobed ductless gland so situated that there is a lobe on each side of the trachea. It manufactures a secretion that is absorbed by the blood and carried about the body. The active principle of the secretion is an organic compound containing iodine and known as *iodothyroglobulin* and *iodothyrin*.

Dose 1–10 grs. (0.06–0.6 gm.).

The uses of thyroid extract will be better understood if the results of abnormal functioning of the gland are recalled. It will be remembered that **inactivity of the gland** in a child results in decrease in the growth of the bones in length, but not in thickness, so that the child is stunted; also, the skull becomes misshapen; the sexual organs do not develop; mental deficiency is marked, and the pituitary gland becomes enlarged, because the body conditions induced by the lack of thyroid secretion stimulate the pituitary gland to increased activity.

The conditions produced in the adult by deficient secretion are: Muscular weakness, mental apathy, thickened skin that has a waxy appearance and is generally cold and dry; the hair falls out and a peculiar edema develops under

the skin and mucous membranes which gives an appearance of obesity to the body; the sexual organs are so affected that menorrhagia is common in women and impotence in men.

In thyroidism—excessive activity of the thyroid—there is usually rapid wasting of the tissues and consequent emaciation; excessive nervousness; sleeplessness; tachycardia; digestive disturbances; diarrhea; diuresis; and sometimes exophthalmos (protrusion of the eyeball) as the result of widening of the eyeslits and retraction of the ciliary muscles.

Thus, it can be seen, **a normal quantity of the thyroid secretion is essential** for normal metabolism, and the normal functioning of the nervous system and the organs of generation.

The common therapeutic uses of thyroid extract are: To supply the body with the necessary amount of the active principle of the secretion when the individual's own gland is not functioning properly; to stimulate metabolism and thus overcome conditions such as obesity and rickets.

If thyroid extract is given in too large amounts or when the body does not require it, conditions similar to those caused by over-activity of the gland will develop.

ANTITHYROID PREPARATIONS

Antithyroidin (*Moebius*) consists of blood-serum obtained from sheep whose thyroid glands have been removed.

Dose, 8–15 m. (0.5–1.0 c.c.).

Thyreoidectin is a powder prepared from the dried blood of animals whose thyroid glands have been removed.

Dose, 5–10 grs. (0.3–0.6 gm.). Antithyroid preparations are used to overcome the effects of thyroidism.

PITUITARY PREPARATIONS

These are obtained from the pituitary glands of cattle.

Preparations and dosage:

Pituitary extract (desiocated hypophysis), 1–4 grs. (0.06–2.6 gm.).

Liquor hypophysis, 15 m. (1.0 c.c.).

Pituitrin, 5–15 m. (0.3–1.0 c.c.).

The above preparations are made from the posterior lobe of the gland.

Desiccated pituitary substance, 1–4 grs. (0.06–0.25 gm.), this is made from the anterior lobe of the gland.

Pituitary body desiccated, 1–3 grs. (0.06–0.2 gm.), this is made from the whole gland.

The pituitary, it will be remembered, **is a** two-lobed gland held by a cord-like structure to the under surface of the cerebrum. The structure of the two lobes is different and also the functions of their secretions.

The effects of the secretion of the front lobe is somewhat similar to that of the thyroid gland and the two secretions are thought to be compensatory, to some extent, one to the other for, it has been repeatedly found, when the thyroid gland is removed or is not furnishing sufficient secretion the anterior lobe of the pituitary becomes enlarged and vice versa.

Removal of a portion of this anterior lobe in animals has been followed by decreased growth, the persistence of infantile characteristics, hypertrophy of the thyroid; accumulation of fat, especially in the abdomen; retarded development of the sex organs; decrease in the rate of the heart action and in breathing; diminished excretion of carbon dioxide and, sometimes, glycosuria.

Hypertrophy of the anterior lobe, if it occurs in childhood, gives rise to the condition known as *gigantism* in which the individual grows to an excessive size and there is precocious sexual development followed, after a time, by a decrease in the activity of the sexual organs and mental impairment. If the condition occurs after body growth has ceased, only the feet, hands and features are likely to increase in size. This is known as *acromegaly.*

The therapeutic uses of the anterior lobe extract are: In stunted growth (*dwarfism*); obesity; premature menopause.

The posterior lobe of hypophysis, it has been found, can be removed without causing any marked symptoms, but various experiments have shown that its secretion, known

as *pituitrin* or *hypophysin*, stimulates the heart muscle and plain muscle tissue, especially that of the arterioles, the intestines, uterus and the ducts of the mammary glands. It increases protein catabolism, but appears to lessen the assimilation of sugar, for glycosuria sometimes follows its use. Also, it is thought to antagonize the effects of the anterior lobe on sexual development.

The therapeutic uses of pituitrin were given in the section dealing with drugs that obtain their chief effects by stimulating plain muscle tissue.

OVARIAN EXTRACT

Ovarian extract is a powder prepared from the ovaries of animals, usually pigs.

Dose 1–3 grs. (0.06–0.2 gm.).

The internal secretion of the ovaries (in the female) and the testes (in the male), it is believed, exercise a direct influence on metabolism by increasing the oxidative energy of cells, thus favoring catabolism. There is also almost conclusive evidence that the differences in the sex characteristics are due to a very considerable degree to the specific actions of these two secretions. The ovarian secretion also influences the condition of the uterus and menstruation.

Ovarian extract is used chiefly in the treatment of: Circulatory and nervous disturbances that occur at the menopause and following removal of the ovaries; amenorrhea; dysmenorrhea; headache, nervousness and abnormal conditions due to irregular menses; sterility.

CORPUS LUTEUM EXTRACT AND LUTEIN

Corpus luteum extract is prepared from the corpora lutea of cows' ovaries.

Dose 2–5 grs. (0.13–0.3 gm.).

Lutein is prepared from the corpora lutea of hogs.

Dose 2–10 grs. (0.13–0.6 gm.).

The corpus luteum, it will be remembered, is the temporary glandular structure that forms in the Graafian

follicle after the escape of an ovum and undergoes marked development when pregnancy occurs. The secretion of the corpus luteum influences the uterine mucosa, bringing about the changes that occur in menstruation, thus preparing the mucosa for the embedding of an ovum. Also, it has been suggested, that in pregnancy, this secretion may overcome the characteristic nausea, because this ceases when the glandular structure reaches its acme of development.

Corpus luteum extract and lutein are used chiefly: To relieve the nervous conditions associated with the menopause; to overcome dysmenorrhea and amenorrhea; and persistent vomiting, especially during pregnancy.

Following large doses and, sometimes, even small ones there may be intense headache and, if given by mouth, excessive nausea and vomiting.

PLACENTAL EXTRACT

Desiccated placenta is used as a galactagogue, *i.e.*, to increase the secretion of milk.

MAMMARY SUBSTANCE

This is prepared from the mammary gland of sheep, it is said to have an effect on the uterus which lessens menorrhagia (abnormally profuse menstruation).

Dose 2–5 grs. (0.13–0.3 gm.) or 1–3 pills.

PARATHYROID AND THYMUS GLANDS

Other glands of which extracts are being tested to ascertain their value in the treatment of conditions which, apparently, their secretions prevent are the parathyroids and the thymus.

Dose desiccated parathyroid, $\frac{1}{10}$ gr. (0.006 gm.).

The parathyroids are small glandular bodies lying in close proximity to the thyroid gland. Their function is not understood, but they are thought to yield a secretion that in some way controls metabolism and the use of the calcium salts by the nerve and muscular tissues, because, it has been found, when the glands are removed,

the elimination of calcium is increased and the condition known as tetany induced. Tetany is characterized by hyper-excitability of the neuro-muscular mechanism and consequent spasmodic contractions of muscles, and calcium is known to lessen neuro-muscular excitability.

The thymus is a gland situated in the chest, behind the sternum. It gradually atrophies after puberty. When it is removed in young animals there will be: imperfect growth and defective calcification of the bones, abnormal deposits of fat in different parts of the body; instability of the nervous system with tremors or convulsions and, finally death. It is thought that after puberty the other glands, especially the parathyroids compensate the body for the gradual inactivity of the thymus.

For preparations of the suprarenal capsules see Epinephrine, pages 197 to 201.

Thromboplastic Substances.—The so-called *thromboplastic substances are preparations used* to hasten the clotting of blood. It will be remembered that the *clotting of blood depends upon* the change of the soluble fibrinogen of the blood to the insoluble fibrin which change is brought about by a substance known as *thrombin* that is developed from a substance known as *prothrombin* by the action of the calcium salts of the blood and a substance termed *thrombokinase* and *thromboplastin*, which is liberated chiefly from red blood platelets when they are destroyed, but also, under the same circumstance, from other tissue cells, especially those containing what is known as *phosphated kephalin*, a substance that is particularly abundant in the brain and spinal cord.

The thromboplastic preparations in common use are: Brain extract. Brain lipoid. Kephalin. Thromboplastin. Coagulen. The four first mentioned preparations are made from the brain or spinal cord of cattle and coagulen from red-blood platelets. They are generally used locally, being sprayed over the bleeding part or applied on a dressing, but they are sometimes given intravenously or intramuscularly.

NUTRIENTS

Certain foods that are made use of in the treatment of disease are sometimes considered with drugs. These are: (1) Foods specially prepared for the use of diabetics; (2) glucose, which is often given by rectum when food cannot be taken by mouth, as a rule, however, it can only be given in this way in dilute solution, about 5 cent., and in small quantities at a time, 5–6 ounces, because large amounts and stronger concentrations cause irritation and consequent expulsion of the solution; (3) partially digested foods, such as (*a*) the malt extracts mentioned on page 116, (*b*) milk preparations such as kumyss, matzoon, etc. (*c*) digested meat products, such as peptones, used in nutritive enemata, and panopepton, a preparation of beef and wheat predigested with pancreatin and dissolved in sherry, dose ½ ounce; (4) cod-liver oil.

Cod-liver oil (*oleum morrhuae*), which is extracted from the livers of codfish, is the only one of the above nutrients not described in text-books of dietetics. The oil, partly because of its disagreeable flavor and odor and partly because it was formerly supposed to owe its very decided nutritional value to the iodine, chlorides, phosphates and similar compounds which it contains, has always been considered as a medicine rather than a food, but it is now believed that the various medicinal substances are present in too minute quantities to be of any therapeutic value and that the improvement in nutrition which so often follows the use of cod-liver oil is due to the fact that the oil is an easily digested and readily assimilated fat that contains a larger amount of the vitamine which is particularly essential for growth and the prevention of rickets than most foods, except cream and good, fresh butter.[1]

[1] See foot-note, page 238.

Preparations and dosage:

Cod-liver oil, 1–2ʒ (4.0–8.0 c.c.).

Emulsion of cod-liver oil, 2–4ʒ (8.0–16.0 c.c.). This is a 50 per cent. preparation of the oil in acacia, flavored with wintergreen and sugar.

There are also a number of non-official preparations of the oil with other substances and of so-called extracts, but, it is believed that if any of the latter preparations have good effects they owe them to their other constituents as the oil contains no valuable extractive matter.

OXYGEN

The oxygen required by the body to maintain the oxidative processes necessary for life is absorbed by the hemoglobin of the red corpuscles as the blood is flowing through the lungs. A very small amount of oxygen, about 0.6 per cent., may go into simple solution in the blood, but oxygen is not very soluble in blood plasma. The amount of oxygen that hemoglobin can combine with is limited but, up to the limit of the latter's capacity, the degree of pressure that the oxygen exerts is, under normal conditions, the main factor in determining the amount of combination. The degree of pressure that the oxygen exerts depends, of course, upon the quantity inhaled. Under ordinary circumstances, except at high altitudes (where atmospheric pressure is diminished) and in very badly ventilated buildings, the amount of air inhaled contains as much oxygen as the hemoglobin can combine with and this, if the amount of hemoglobin is normal and there is nothing to interfere with its combining power, is as much oxygen as the body can utilize. Conditions which interfere with the power of the hemoglobin to combine with oxygen are, reduced alkalescence of the blood and changes in the nature of the hemoglobin such as occur in poisoning by carbon monoxide gas and in poisoning by drugs that change the hemoglobin to methemoglobin.

When conditions exist that interfere with breathing, or with the ready diffusion of air through the lungs, or with the power of the hemoglobin to absorb oxygen, pure oxygen given by inhalation may be of great assistance in maintaining life, for it diffuses more readily through the lungs and the walls of the alveoli into the blood than when, as in air, it is mixed with nitrogen, also, it is believed, that, due to the increased pressure, a greater amount than usual goes into solution in the blood.

Inhalation of pure oxygen is likely to induce slowing of the heart action and a slight rise of blood pressure. These results are believed to be due to reflexes induced by irritation of the mucous membrane by the oxygen, for pure oxygen causes drying of the mucous membrane and irritation. To prevent bad effects from this local action, oxygen is passed through water when it is given by inhalation, for this moistens it and thus lessens its irritant action. Also, when oxygen has to be given for any length of time, a common prescription is to keep the air over the patient's bed moist with steam.

Oxygen is most commonly used in conditions associated with cyanosis and dyspnea, for these phenomena indicate an insufficiency of oxygen in the body. Decrease of these symptoms and slowing and strengthening of the pulse are the indications of beneficial results that are to be watched for.

CLASSIFICATION OF THE MORE IMPORTANT DRUGS ACCORDING TO THEIR THERAPEUTIC USES

This classification has been based chiefly on the Therapeutic Index in the 1920 reprint of "Useful Drugs" and on the list of drugs classified according to their therapeutic uses in the seventh edition of "A Text-Book of Pharmacology and Therapeutics," by Arthur R. Cushny. Its principal purpose is to afford a basis for recall and review and the pupils should be required to state how each drug produces the effects for which it is used.

DRUGS APPLIED FOR THEIR LOCAL ACTION TO THE SKIN, WOUNDS OR VISIBLE MUCOUS MEMBRANES

Local analgesics and anodynes for pain and itching:	Aconite. Aqua ammonia. Atropine. Carbolic. Chloretone. Chloroform. Cocaine. Menthol. Orthoform. Sodium bicarbonate. Some volatile oils (in dentistry).
Local anesthetics:	Cold obtained by the evaporation of ether or ethyl chloride. Cocaine. Novocaine. Quinine and urea chloride.
Emollients:	Bland oils, such as olive and cotton seed. Cold creams. Lanolin. Lard. Petroleum. Vaseline.
Protectives:	Starch and dusting powders. Many of the insoluble metallic powders, but especially those of bismuth. Collodion. Wax. Paraffines. Emollients.
Corrosives or caustics:	Glacial acetic acid. Trichloracetic acid. Mineral acids. Carbolic acid. Burnt alum. Silver nitrate. Arsenious acid and arsenious anhydride. Ammoniated mercury. Potassium carbonate. Potassium hydroxide. Sodium carbonate. Sodium hydroxide. Zinc chloride.

Astringents:	Alcohol. Alum. Aluminium acetate. Bismuth preparations. Copper sulphate. Iron preparations. Lead acetate. Silver nitrate. Zinc chloride.
Styptics:	Burnt alum. Iron perchloride. Silver nitrate.
To contract vessels and reduce hemorrhage and swelling:	Adrenaline.
Antiseptics and disinfectants:	See page 380.

DRUGS USED FOR AFFECTIONS OF THE ALIMENTARY TRACT

Mouth and throat:	
Demulcents:	Acacia. Tragacanth. Syrups. Glycerine.
Flavoring substances:	Citric acid. Volatile oils. Spices. Syrup of Tolu. Saccharine. Sugars. Glycyrrhiza.
Astringents:	Tannin group. Chlorates. Claret. Myrrh.
Antiseptics:	See page 380.
To lessen salivation:	Atropine.
Stomach:	
Digestives:	Hydrochloric acid. Pepsin.
To stimulate secretion:	The bitters: Cinchona, Quinine. Gentian. Nux vomica. Strychnine.
Carminatives:	Alcoholic beverages. Camphor. Chloroform. Ether. Capsicum. Spices. Volatile oils such as cardamom, peppermint, turpentine, asafœtida. Carbonated beverages. Carbonates and bicarbonates. For infants, anise and peppermint water.
Absorbents:	Charcoal. Kaolin.
Antacids:	Potassium and sodium carbonates and hydroxides. Magnesia. Magnesium carbonate. Lime-water. Chalk.
Emetics:	Common salt. Warm water. Mustard. Ipecacuanha. Tartar emetic. Copper sulphate. Zinc sulphate. Apomorphine.
To lessen irritation and vomiting:	Bromides. Chloral. Chloretone. Morphine. Opium. Bismuth. Carbonated beverages. Demulcents. Lime-water. Ice. Cocaine.

Intestine:	
Absorbents:	As on page 406.
Antiseptics:	See page 380.
Anthelmintics:	See page 287.
Carminatives:	As above. Also physostigmine and pituitrin.
To promote evacuation:	See list of cathartics on pages 257–260.
To lessen movement:	Opium. Morphine. Tannic acid and its compounds. Bismuth. Lime-water. Lead acetate. Boiled starch.
To relax spasms:	Atropine and, especially combined with cathartics, volatile oils (see page 283).
To promote digestion:	Pancreatin. Diastase.

DRUGS USED FOR THEIR EFFECTS ON THE RESPIRATORY SYSTEM

To stimulate the respiratory center:	Atropine. Carbon dioxide 5–10 per cent. with oxygen. Caffeine. Strychnine.
To reduce the irritability of the cough center:	Bromides of the alkalies. Chloral series. Codeine. Heroine. Morphine.
To increase and liquefy the bronchial secretion (expectorants):	Ammonium carbonate. Apomorphine. Iodides of the alkalies. Ipecacuanha. Eucalyptus. Senega. Squills. Tartar emetic.
To lessen the secretion of the bronchi:	Ammonium chloride. Balsam of Tolu. Benzoic acid. Benzoin. Terpin hydrate.
To relax bronchial spasm in asthma:	Adrenaline. Amyl nitrate. Nitroglycerine. Atropine. Belladonna. Stramonium. Cubebs. Lobelia. Iodides.

DRUGS USED FOR THEIR EFFECTS ON THE NERVOUS SYSTEM

Stimulants:	
Of spinal cord:	Strychnine.
Of medulla and cerebrum:	Caffeine.
Depressants:	
To paralyze sensation:	General anesthetics.
To induce sleep and rest:	Hypnotics mentioned, pages 132 and 136–140.
To relieve pain:	The analgesics mentioned on pages 144–147 and 157. The salicylic acid group. Local anesthetics and anodynes, mentioned on pages 176 and 182–185.

In epilepsy:	Bromides.
To relieve headache:	Analgesic antipyretics. Acetylsalicylic acid (aspirin). Caffeine. Quinine. Menthol (externally).
To relieve cerebral congestion:	Nitrite group. Hydragogue cathartics.
In cerebral anemia:	Adrenaline. Pituitary extract. Digitalis group.

DRUGS USED FOR THEIR EFFECTS ON THE CIRCULATION

By effects on the heart:	
To strengthen contraction:	Digitalis group and camphor.
To accelerate pulse:	Atropine. Caffeine.
To slow the pulse:	Digitalis group. Aconite.
By effects on the vessels:	
To contract caliber and raise blood-pressure:	Adrenaline (intravenously). Digitalis. Caffeine. Ergotoxin. Pituitary extract. Strychnine.
To relax vessels and lower blood-pressure:	Nitrite series. Hydragogues.
To arrest internal hemorrhage:	Adrenaline. Ergot. Hydrastis. Morphine. Pituitary extract.
To remove fluid, as in dropsy:	Digitalis. Diuretics. Diaphoretics. Hydragogue cathartics.

DRUGS USED FOR THEIR EFFECTS ON THE BLOOD

To increase hemoglobin:	Arsenic. Iron.
To reduce leucocytosis:	Arsenic. Benzol. Quinine.
To increase the number of white cells in the blood:	Leucocyte extract.
To increase the alkali:	Acetates. Citrates. Sodium and potassium carbonates and bicarbonates.

DRUGS USED TO INCREASE THE SECRETIONS OF SWEAT

(Diaphoretics)

Camphor. Ipecac, usually in the form of Dover's powder. Pilocarpine. Sweet spirits of niter. Tartar emetic.

DRUGS USED TO LESSEN DIAPHORESIS

Atropine. Belladonna. Agaricin.

DRUGS USED TO REDUCE FEVER TEMPERATURE

(Antipyretics)

Analgesic antipyretics, see page 157. The salicylic acid group. Quinine.

Drugs Used to Stimulate the Secretion of Bile (Cholagogues)

Salicylic acid. Fel bovis.

Drugs Used for Their Effects on the Urinary Organs

To increase the flow of urine (diuretics):	Caffeine. Theobromine and its compounds. Theophyllin. Theocin. Calomel. Volatile oils mentioned on page 382. Digitalis. Strophanthus. Squills. The nitrites. Pituitary extract. Urea. Sodium, potassium and lithium bicarbonates. Sodium and potassium acetates, citrates and tartrates.
To render the urine less acid:	Potassium acetate, citrate and bicarbonate. Sodium carbonate and bicarbonate.
To render the urine more acid:	Sodium biphosphate. Mineral acids.
To render the urine antiseptic:	See urinary antiseptics, page 382.

Drugs Used for Their Effects on the Uterus

To promote contraction (ecbolics):	Ergot. Pilocarpine. Pituitary extract. Hydrastinine. Quinine.
To increase menstruation (emmenagogues):	Iron. Aloes. Myrrh.
To lessen the menstrual flow:	Hydrastis.
To lessen contractions of the uterus and thus relieve painful menstruation:	Atropine. Analgesics and counter-irritants are also used to relieve pain during menstruation but these do not directly affect the uterus.

Drugs Used on the Skin to Produce Remote Effects

To lessen secretion of milk:	Atropine and belladonna.
For counterirritation:	Ammonia. Camphor. Cantharides. Iodine. Liniments. Mustard. Turpentine. Oils of birch and wintergreen.

Drugs Used Locally for Their Effects on the Eye

To diate the pupils and relax accommodation (mydriatics, cycloplegics).	Atropine. Homatropine. Hyoscine, Cocaine.

To contract the pupils and ciliary muscles (miotics):	Physostigmine or eserine. Pilocarpine.

DRUGS USED FOR SPECIFIC DISEASES

In malaria:	Quinine. Arsenic.
In syphilis:	Arsenic. Mercury. Iodides.
In diphtheria:	Antidiphtheritic serum.
In tetanus:	Antitetanic serum. Bromides. Chloral. Magnesium intraspinally.
In cerebro-spinal fever:	Antimeningococcus serum.
In amœbic dysentery:	Ipecac. Emetine
In rheumatic fever:	Salicylates.
In myxedema and some other thyroid diseases:	Thyroid extract. Iodides.
In gout:	Colchicum. Atophan
In obesity:	Thyroid extract. Saline purgatives.
In chronic rheumatism:	Arsenic. Iodides. Alkalies.
In diseases of the bone such as osteomalacia and rickets:	Calcium. Phosphorus. Arsenic. Thyroid extracts.

NOTES ON NEW DRUGS

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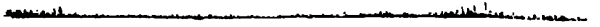

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